Figure 1: Ribozyme Motifs

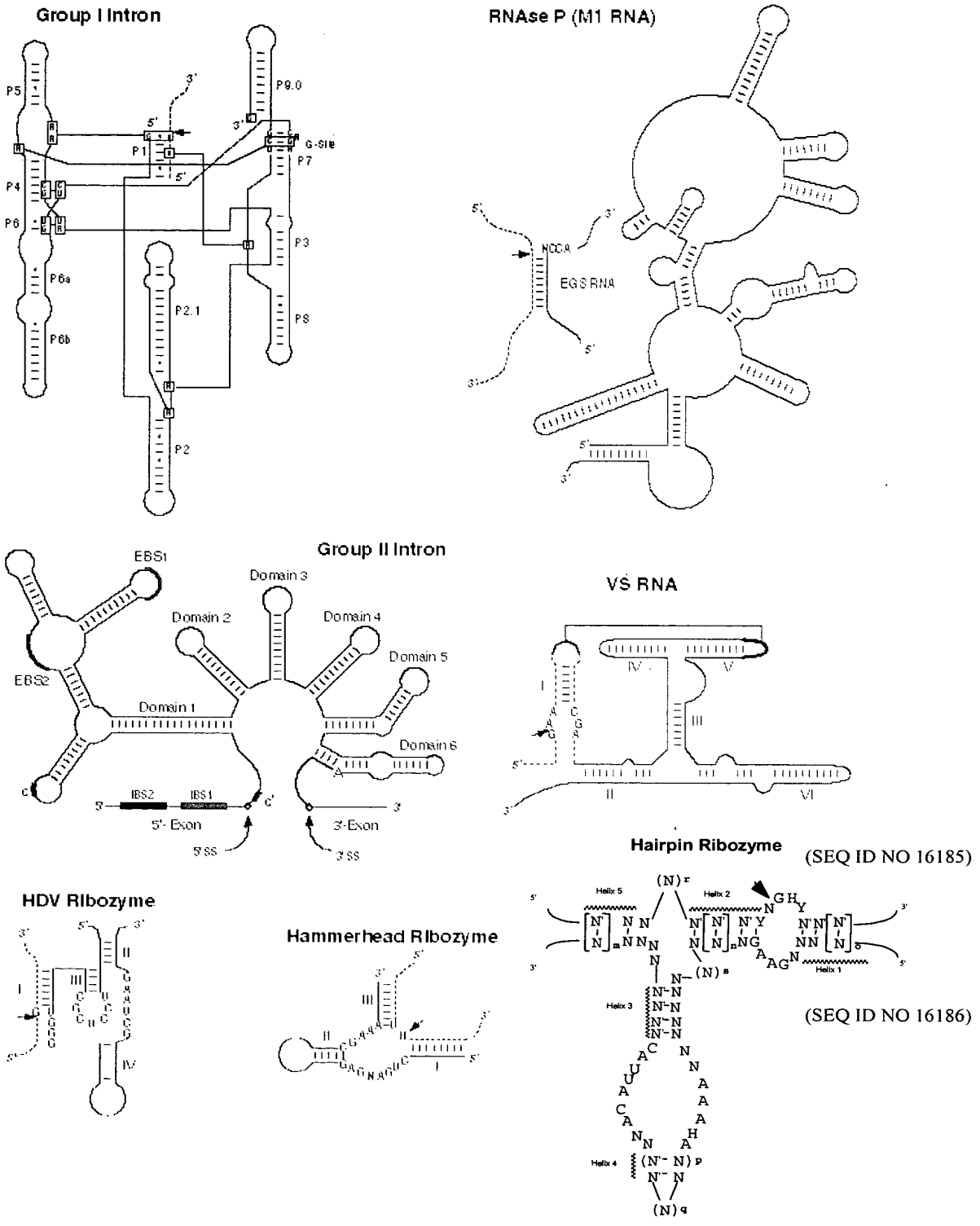


Figure 2: Examples of Nuclease Stable Ribozyme Motifs

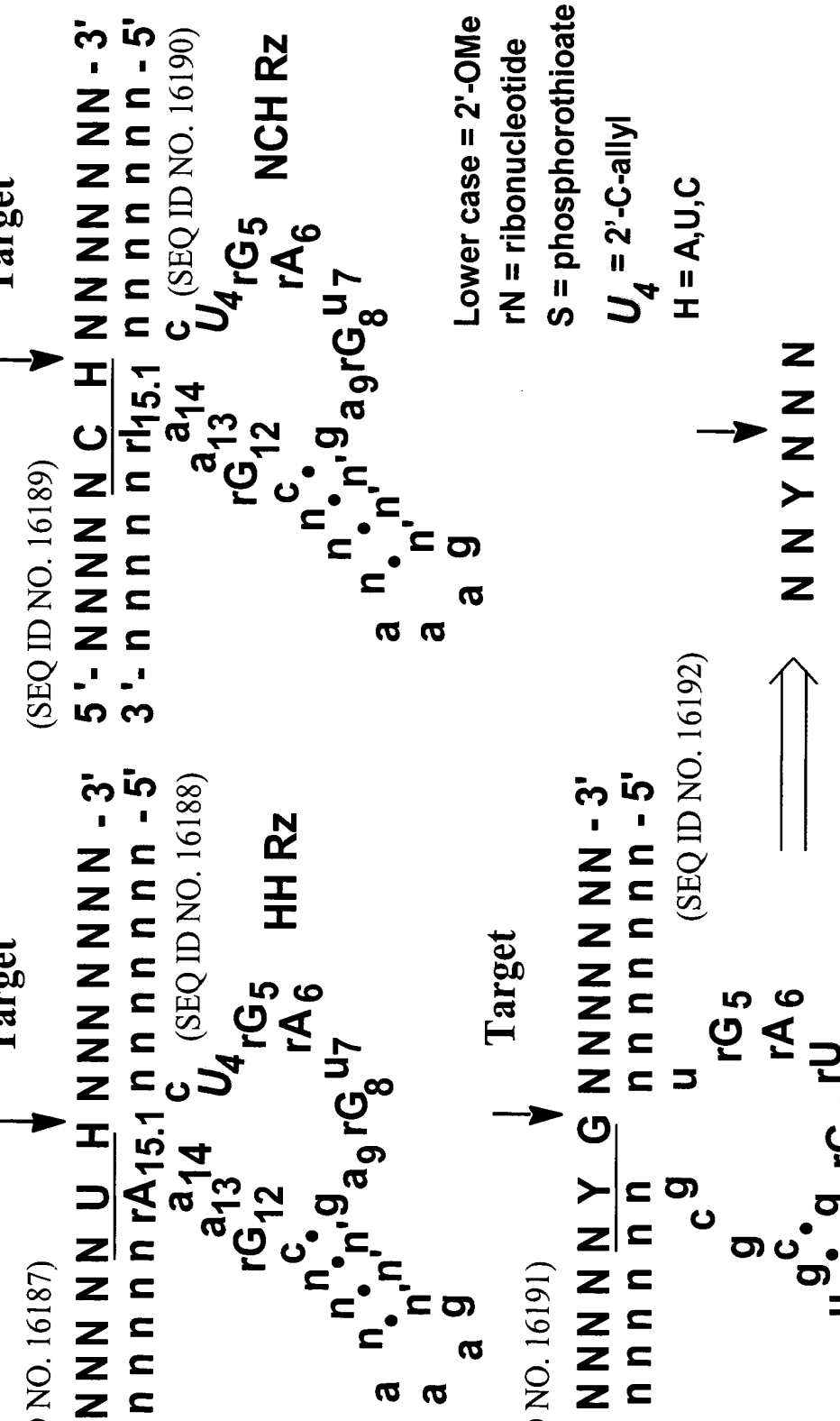


Figure 3: 2'-O-Me substituted Amberzyme Enzymatic Nucleic Acid Motif

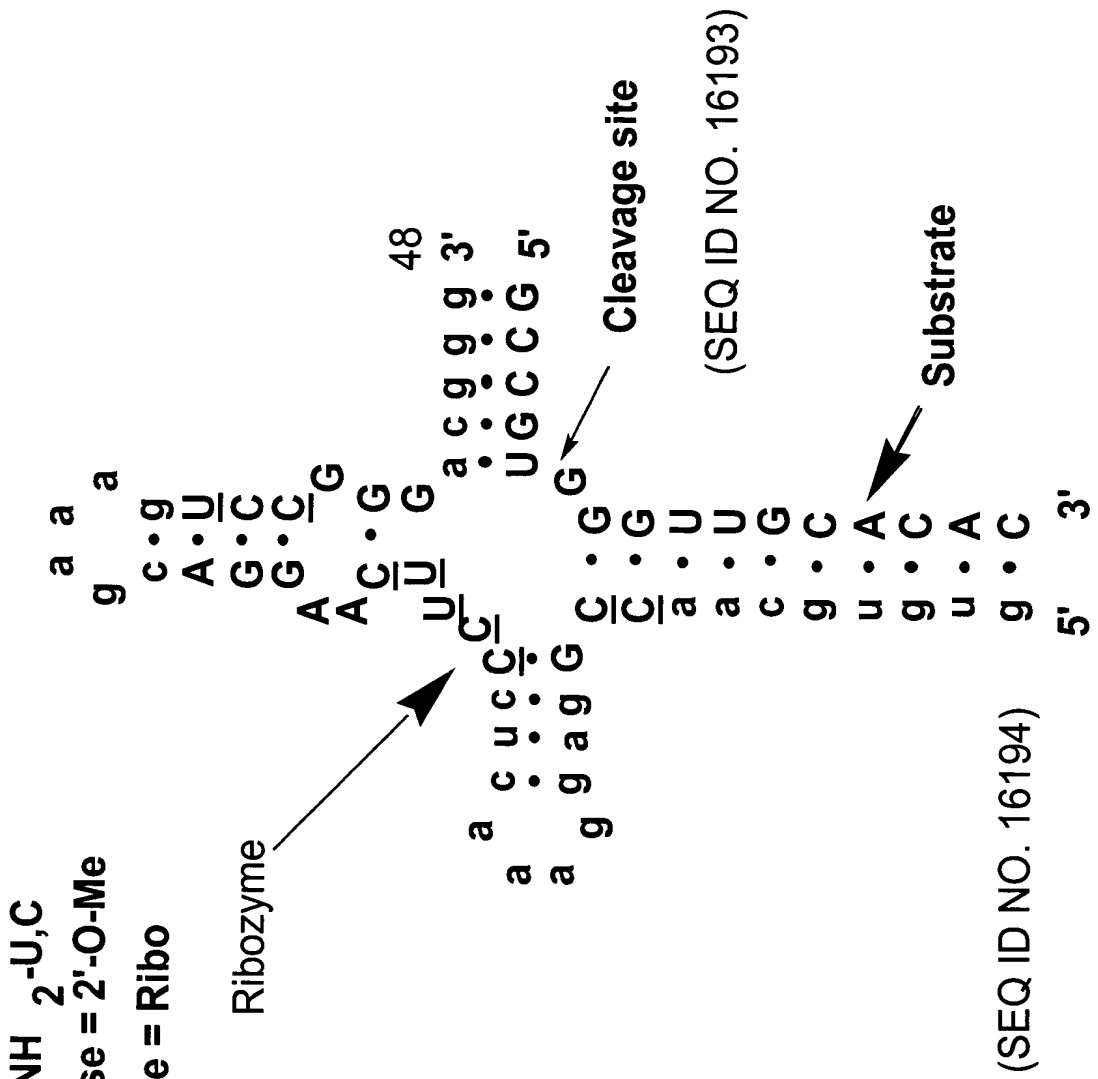
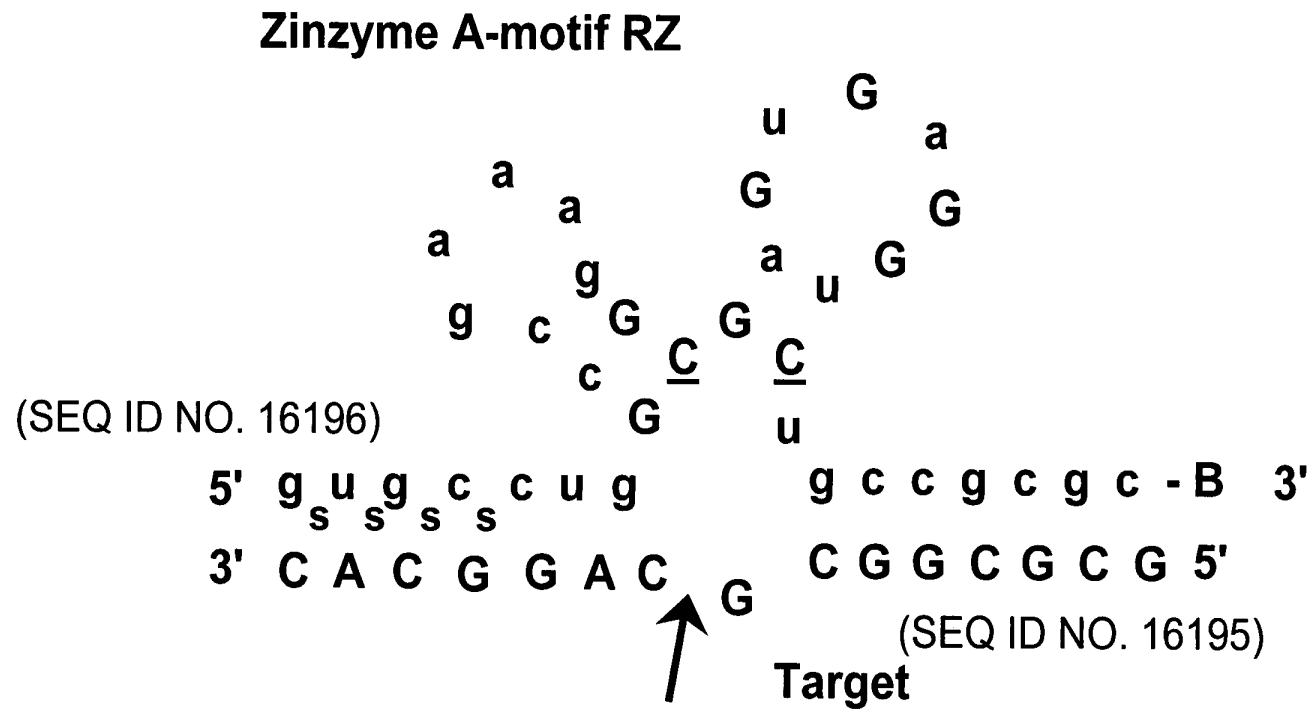


Figure 4: Stabilized Zinzyme Ribozyme Motif



Legend

Uppercase indicates natural ribo residues

C indicates 2'- d-NH_2-C

Lowercase: 2'-O-Me

Subscript $_S$ indicates phosphothioate linkage

B: 3'- 3' abasic moiety

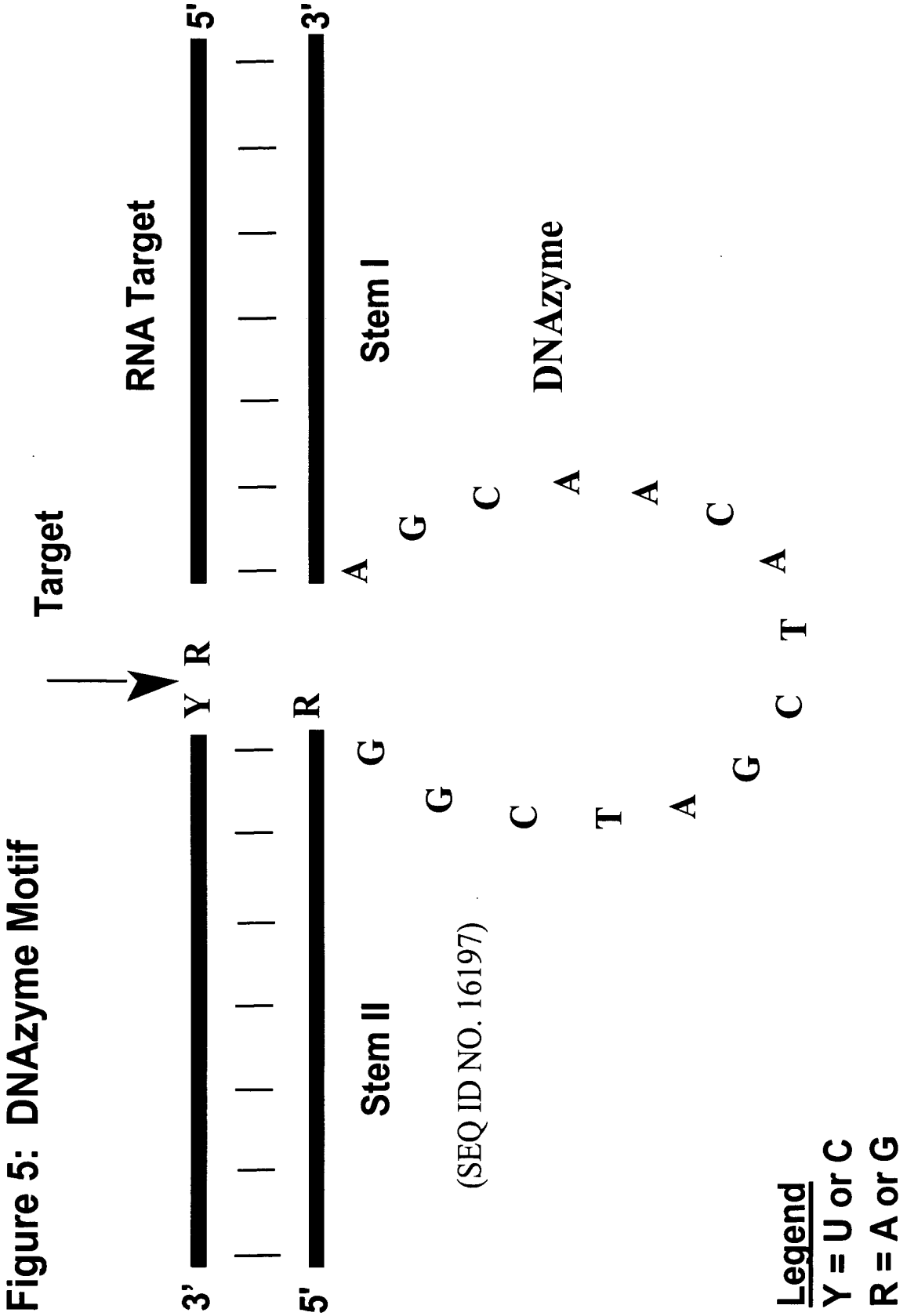


Figure 5: DNAzyme Motif
Target
RNA Target
5'
3'
Y R
Stem I
DNAzyme
A G C A A C A
R
G G C T A G C
Stem II
3'
5'
(SEQ ID NO. 16197)
Legend
Y = U or C
R = A or G

Figure 6: Change in Serum HBV DNA Levels Following 14 Days of Ribozyme Treatment of HBV Transgenic Mice

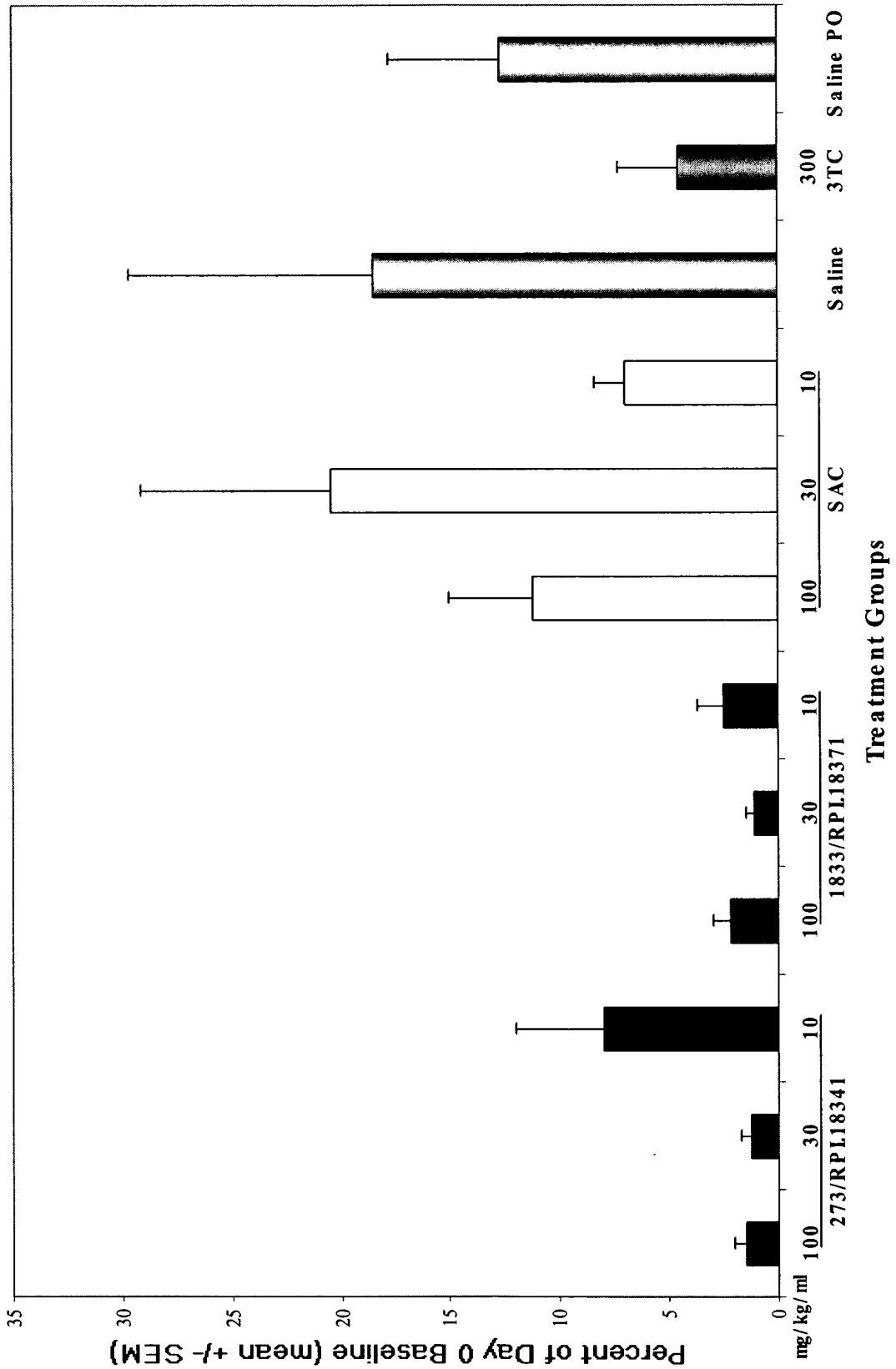


Figure 7: Mean Serum HBV DNA Levels Following 14 Days of Ribozyme Treatment of HBV Transgenic Mice

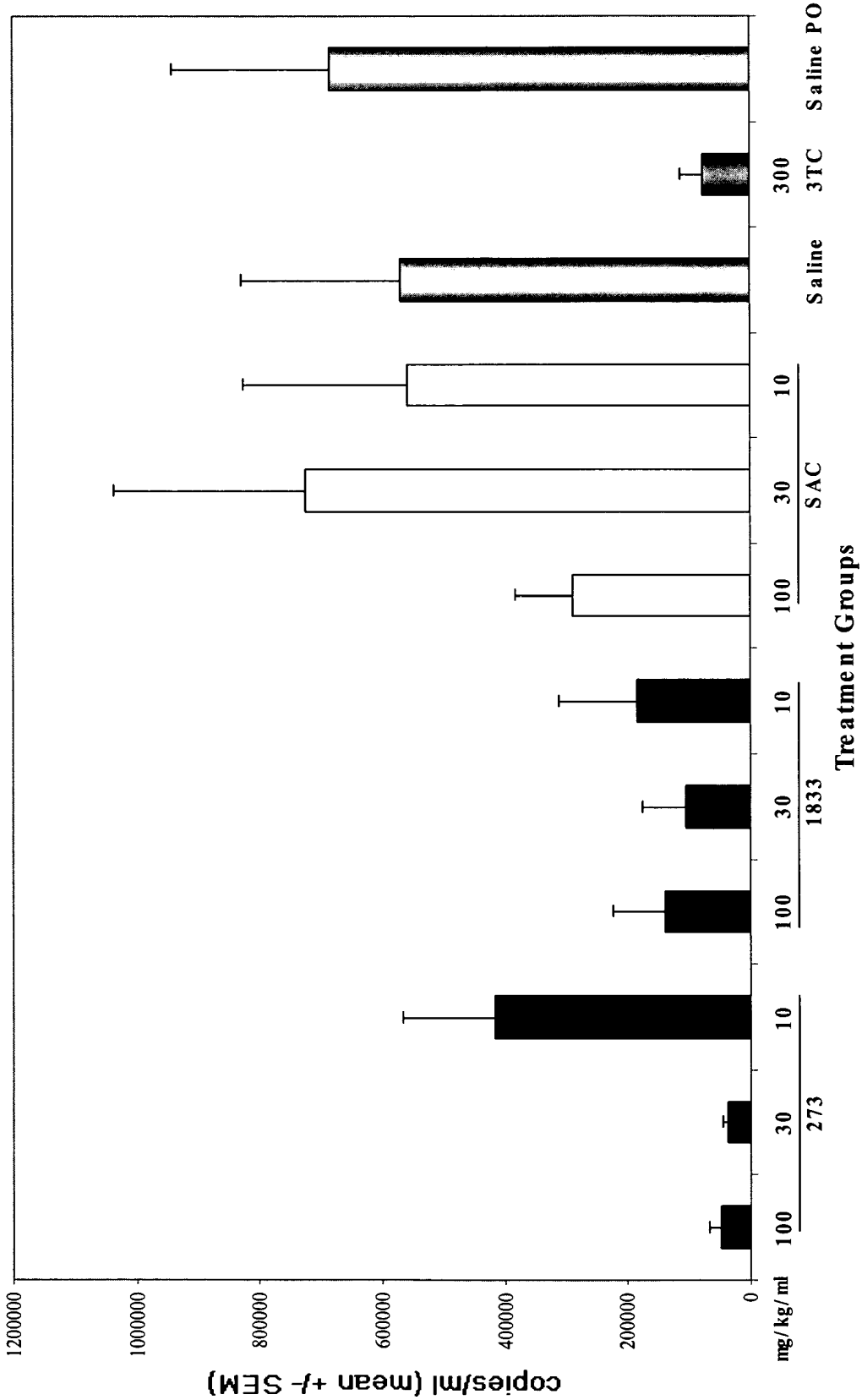


Figure 8: Change in Serum HBV DNA Levels (Log) Following 14 Days of Ribozyme Treatment of HBV Transgenic Mice

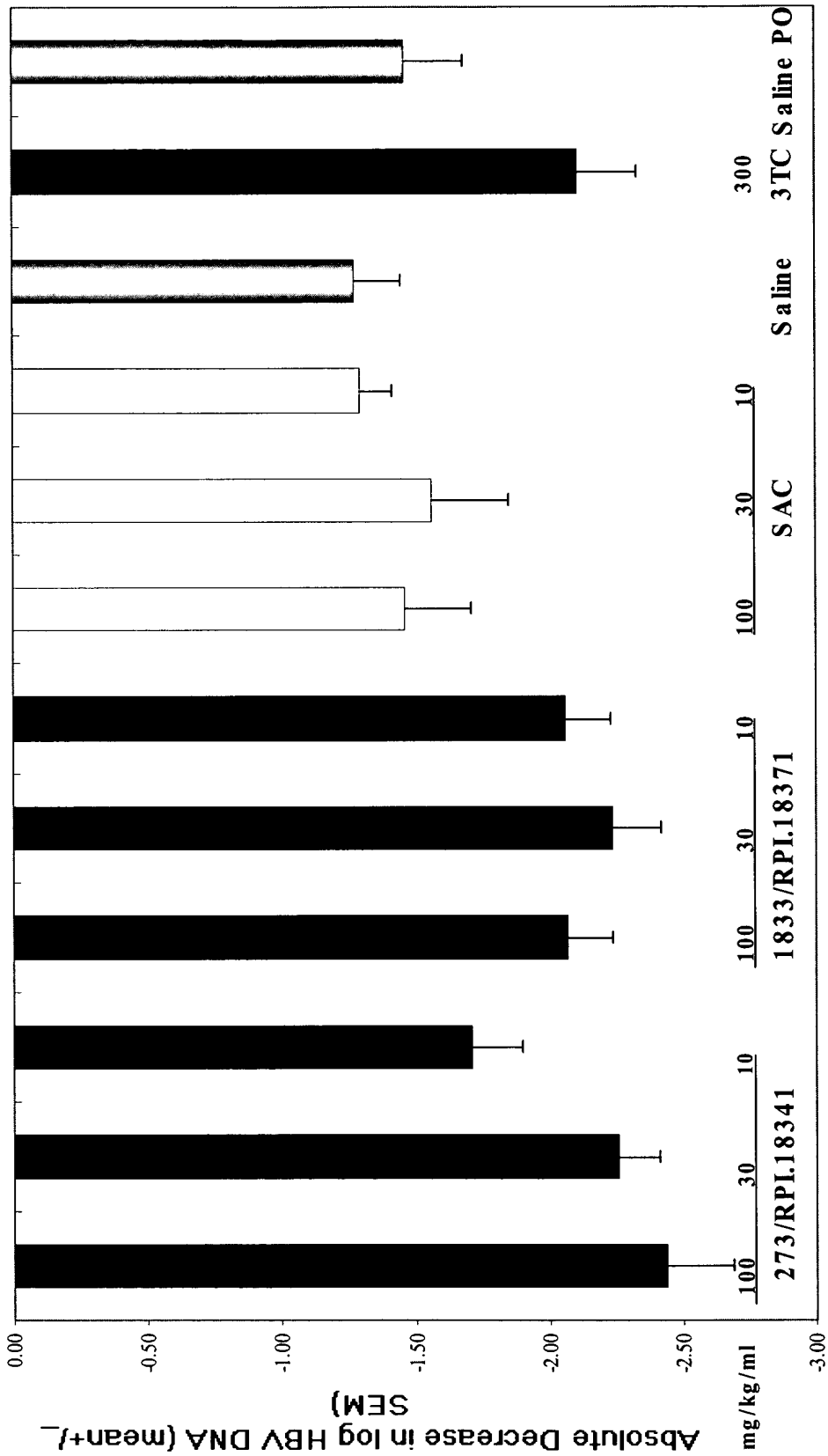


Figure 9: anti-HBV Ribozymes in HepG2.2.15 Cells: HBV DNA

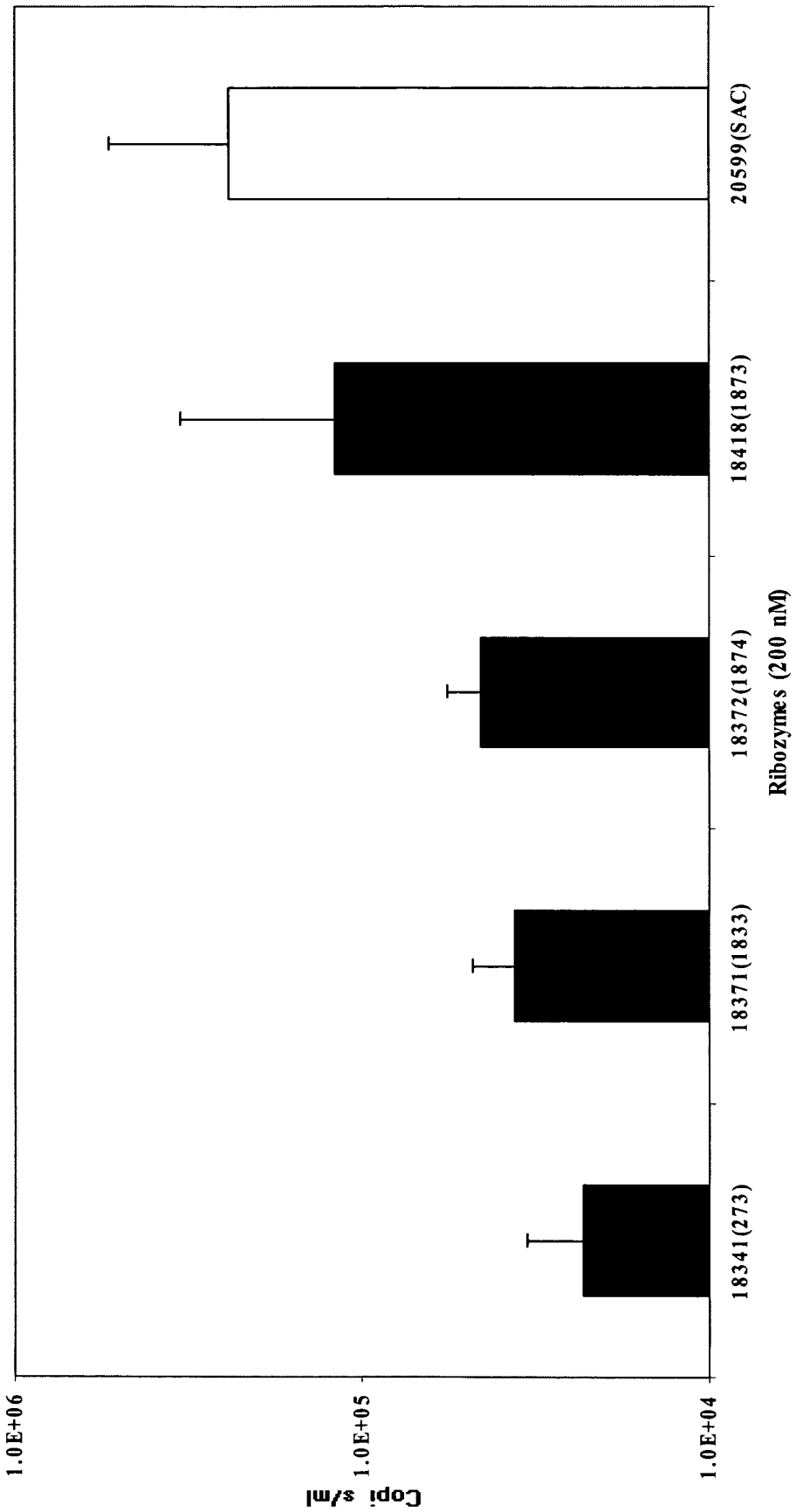


Figure 10: Arm, Loop, and Stem Variants of Anti-HBV Ribozyme Targeting Site 273: HBsAg Levels in Hep G2 Cells

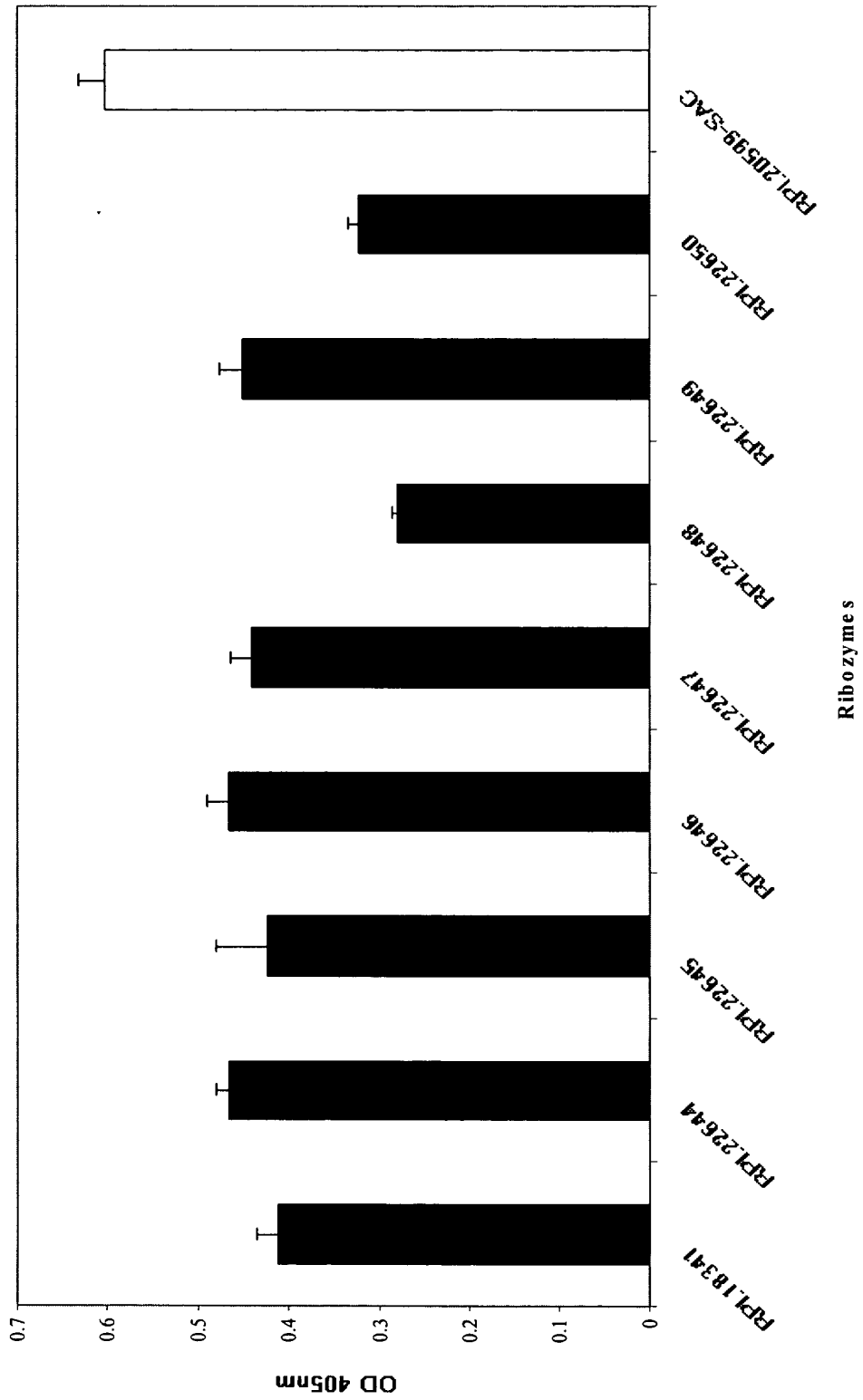


Figure 11: Hep G2 Cells Treated with RPI.18341and Interferon: HBsAg ELISA

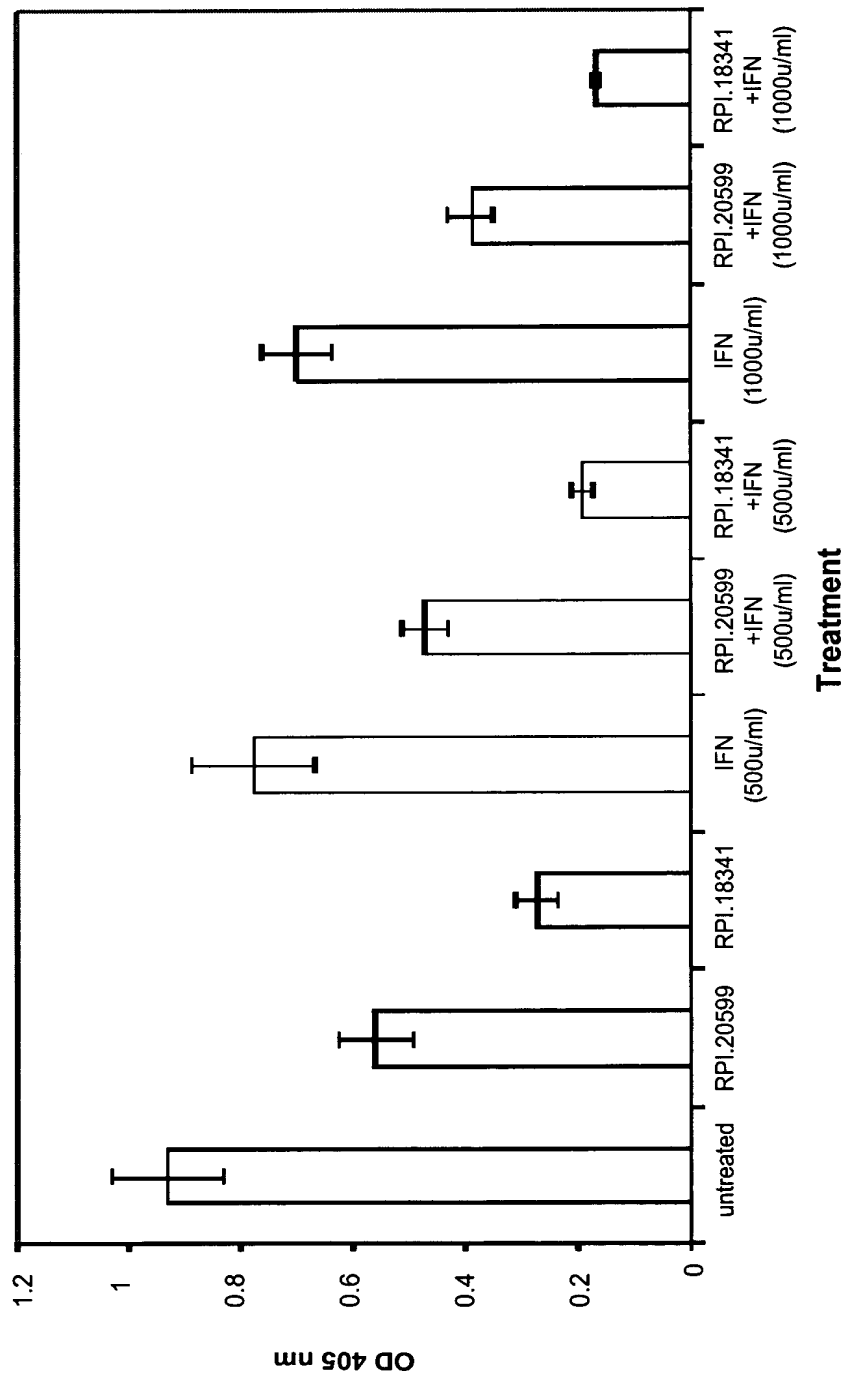


Figure 12: Hep G2 Cells Treated with 100 nM RPI.18341 and Lamivudine (3TC): HBsAg ELISA

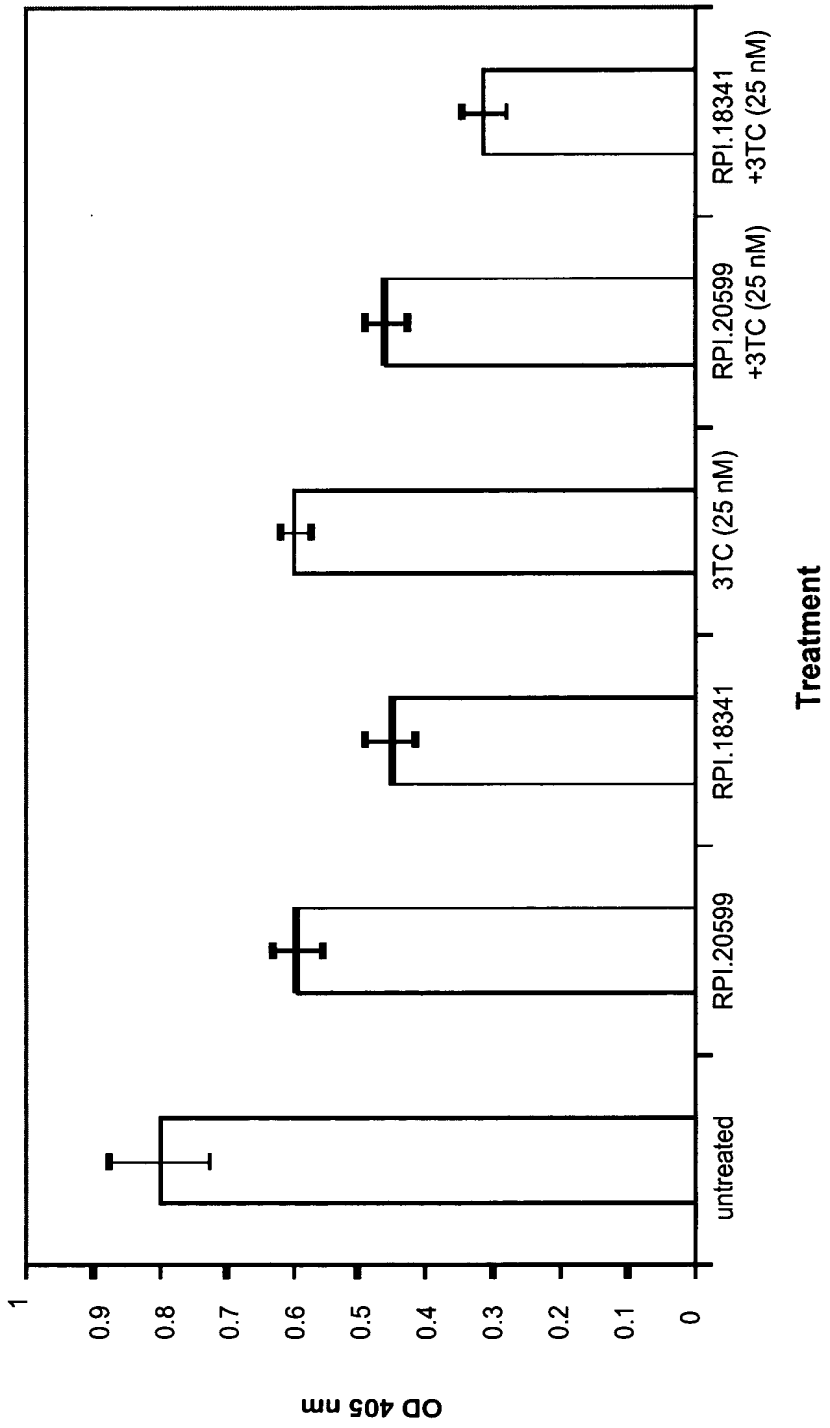


Figure 13: HBV Reverse Transcription

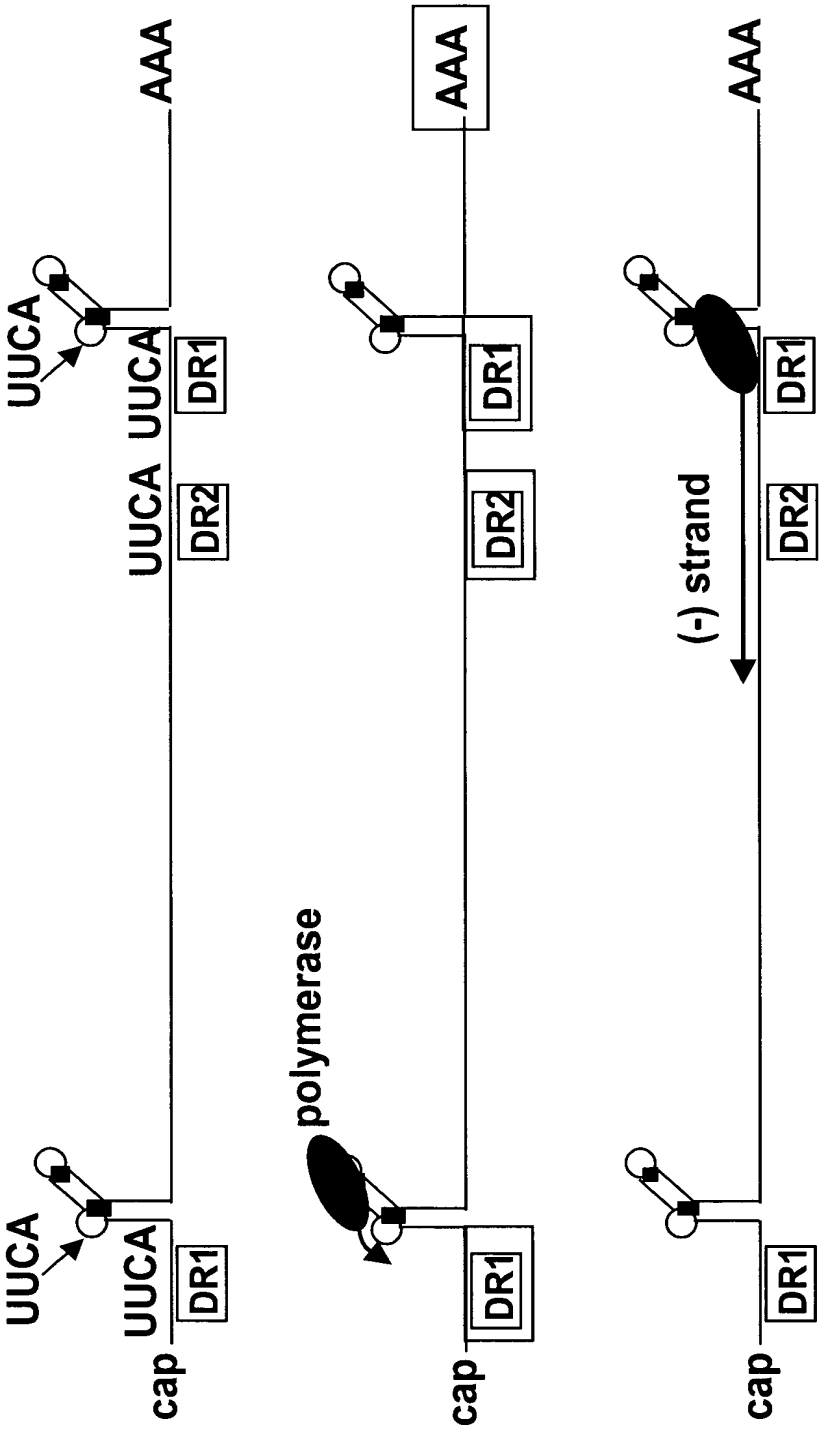


Figure 14: HBV RT Inhibition

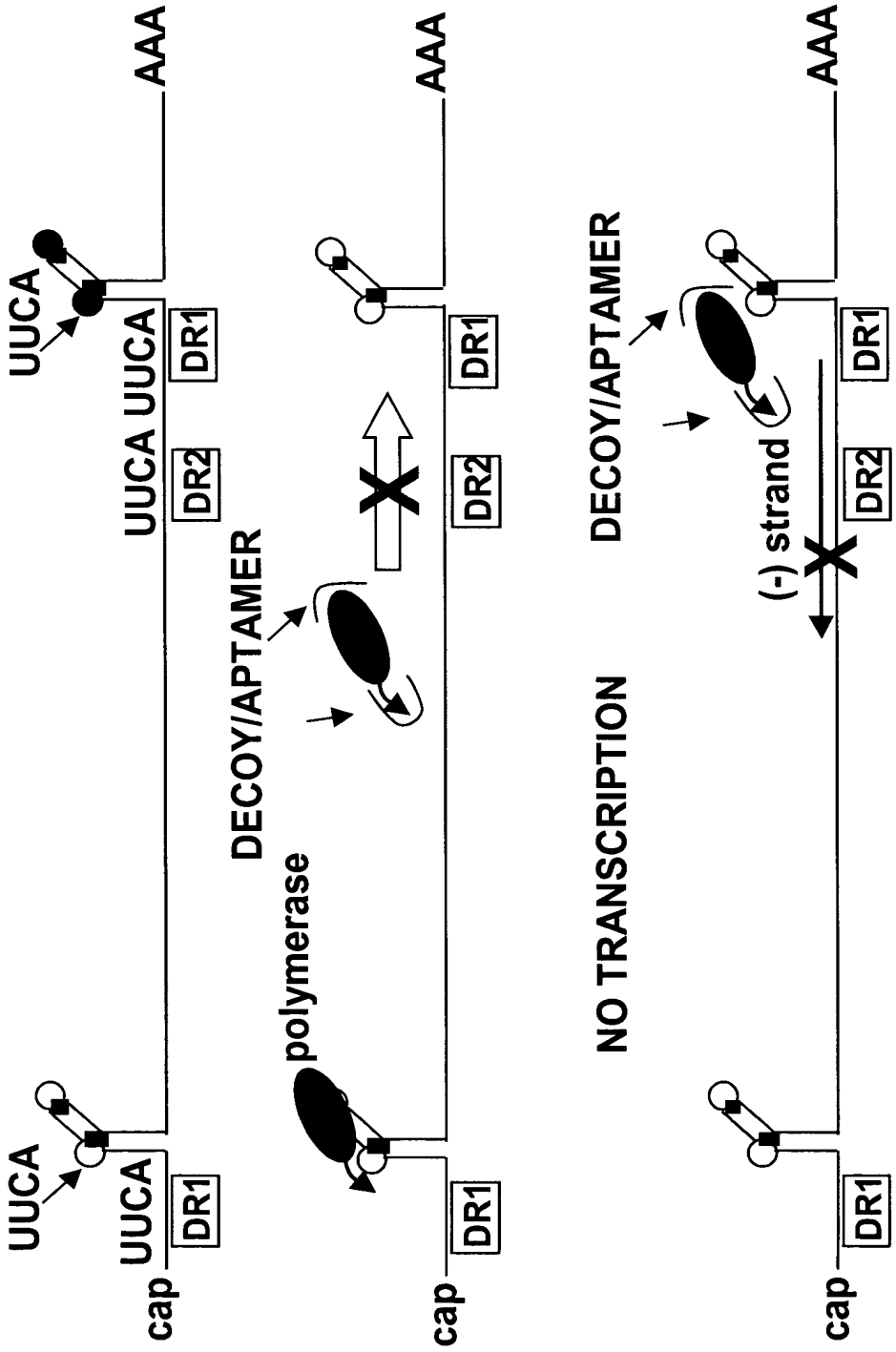


Figure 15: Screening of HBV RT Primer Competitive Inhibitors (2'-O-Allyl): HBsAg

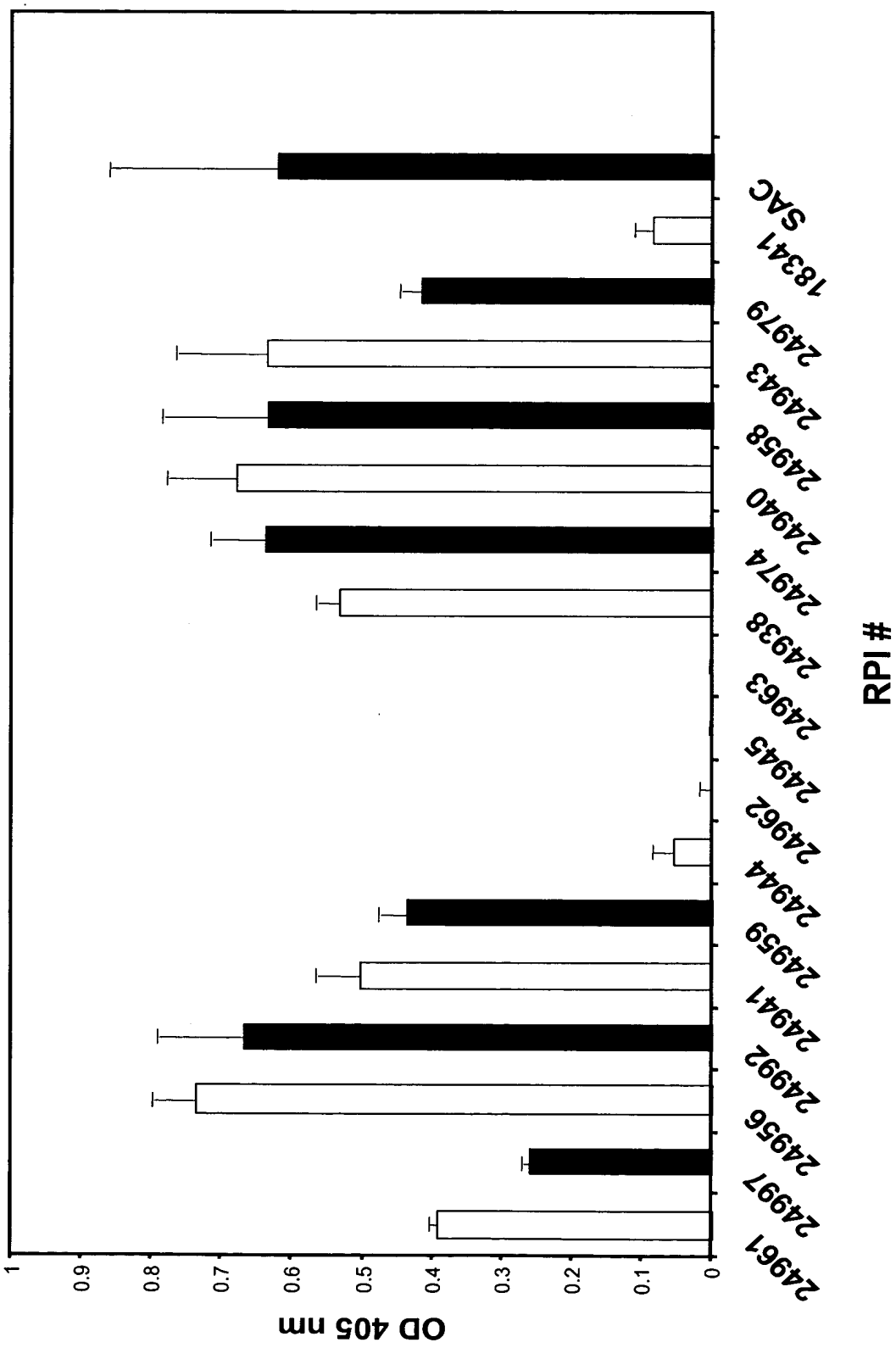


Figure 16: Screening of HBV RT Primer Competitive Inhibitors (2'-O-Methyl): HBsAg

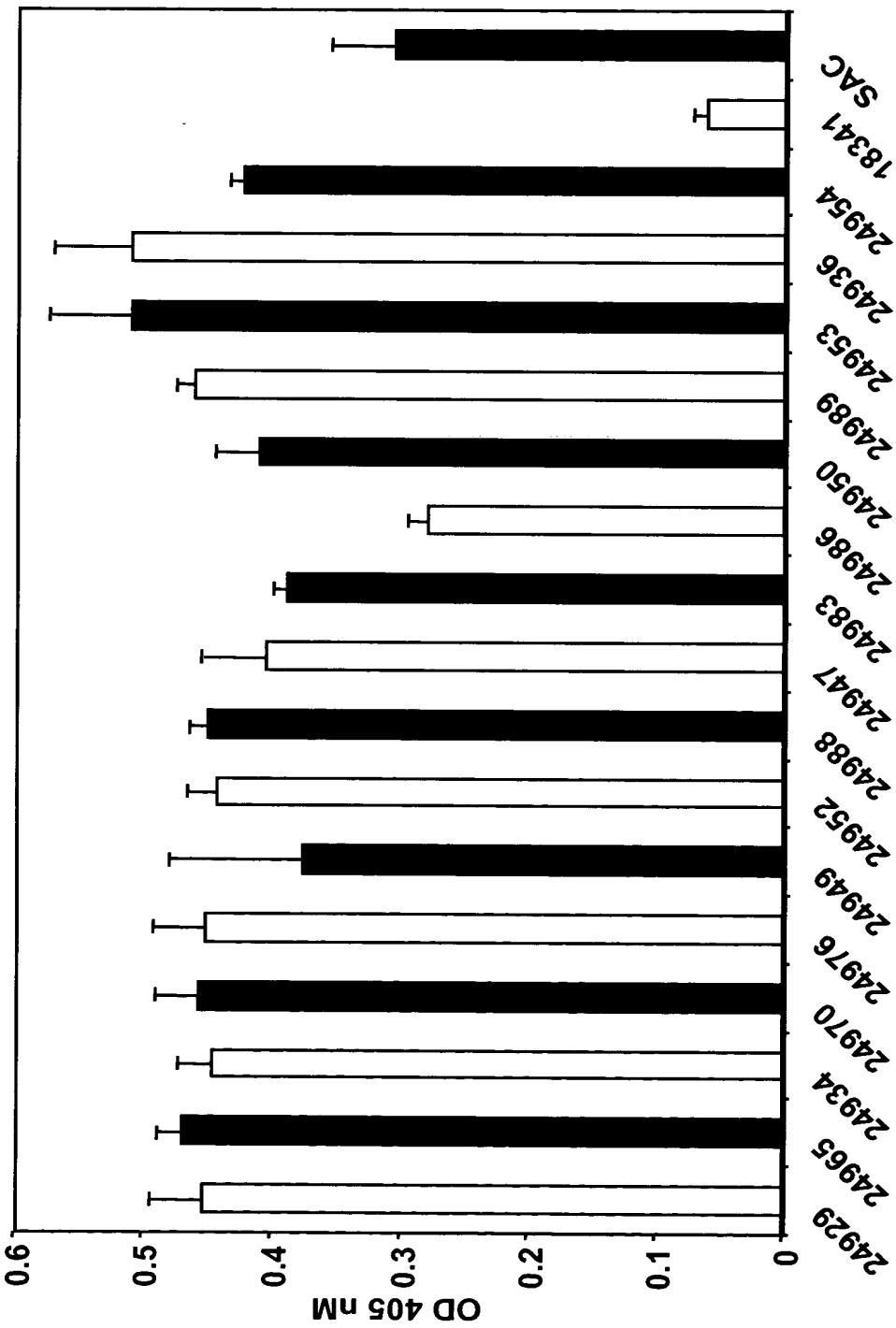
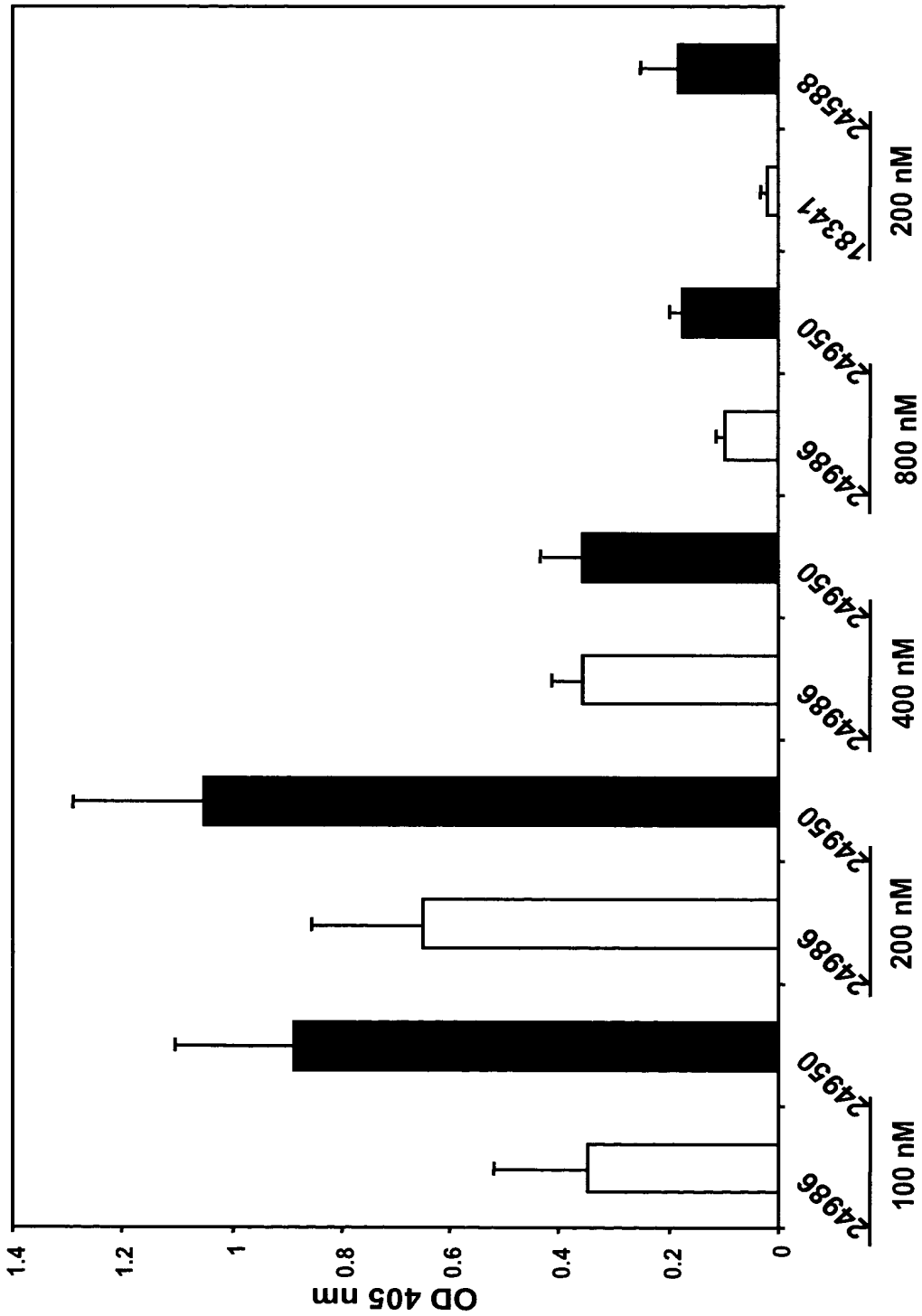


Figure 17: Dose Response with 2'-O-Methyl UUCAUUCA Oligo: HBsAg



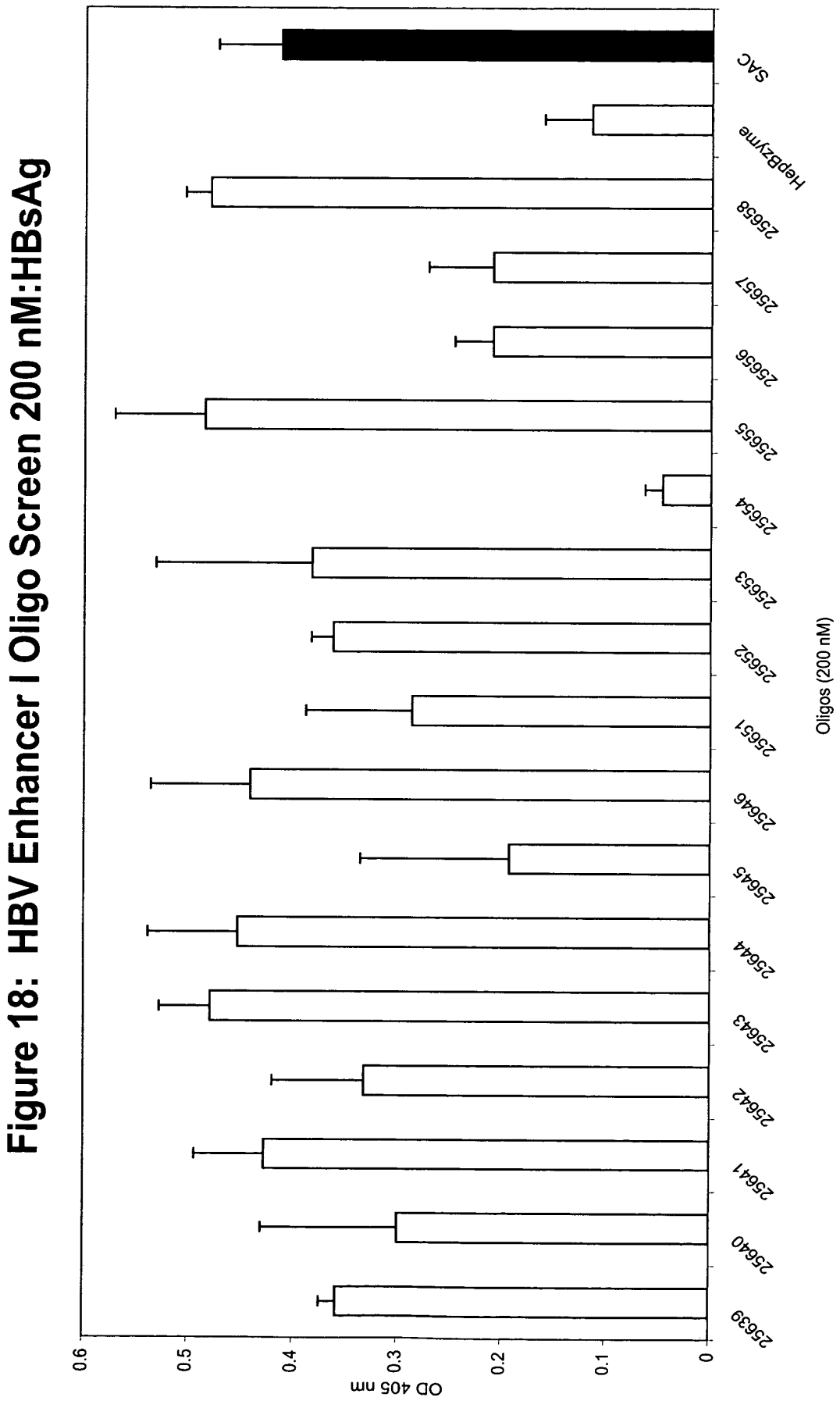


Figure 18: HBV Enhancer I Oligo Screen 200 nM:HBsAg
OD 405 nm
0
0.1
0.2
0.3
0.4
0.5
0.6
Oligos (200 nM)
25639
25640
25641
25642
25643
25644
25645
25646
25651
25652
25653
25654
25655
25656
25657
25658
HepBzyme
SAC

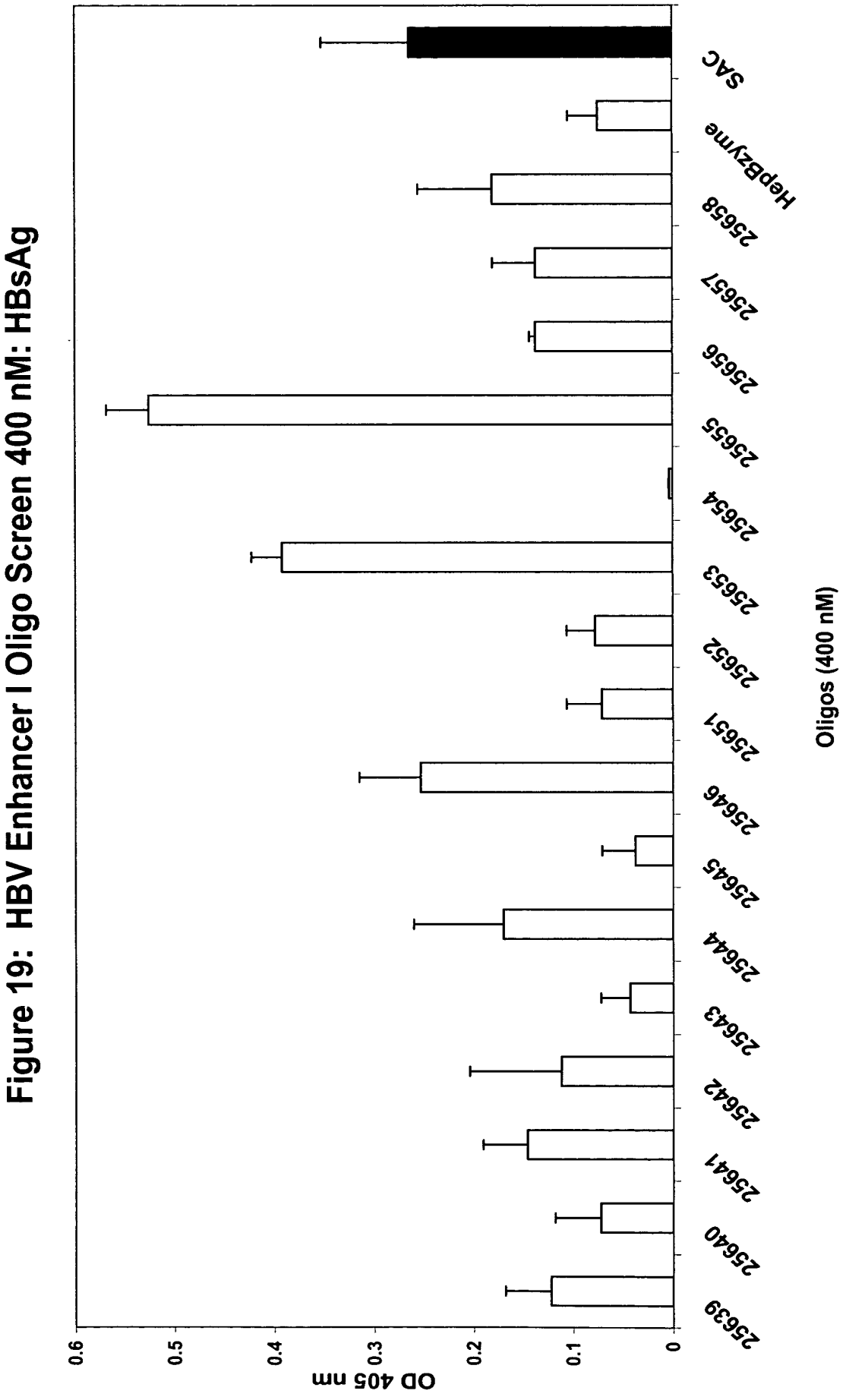
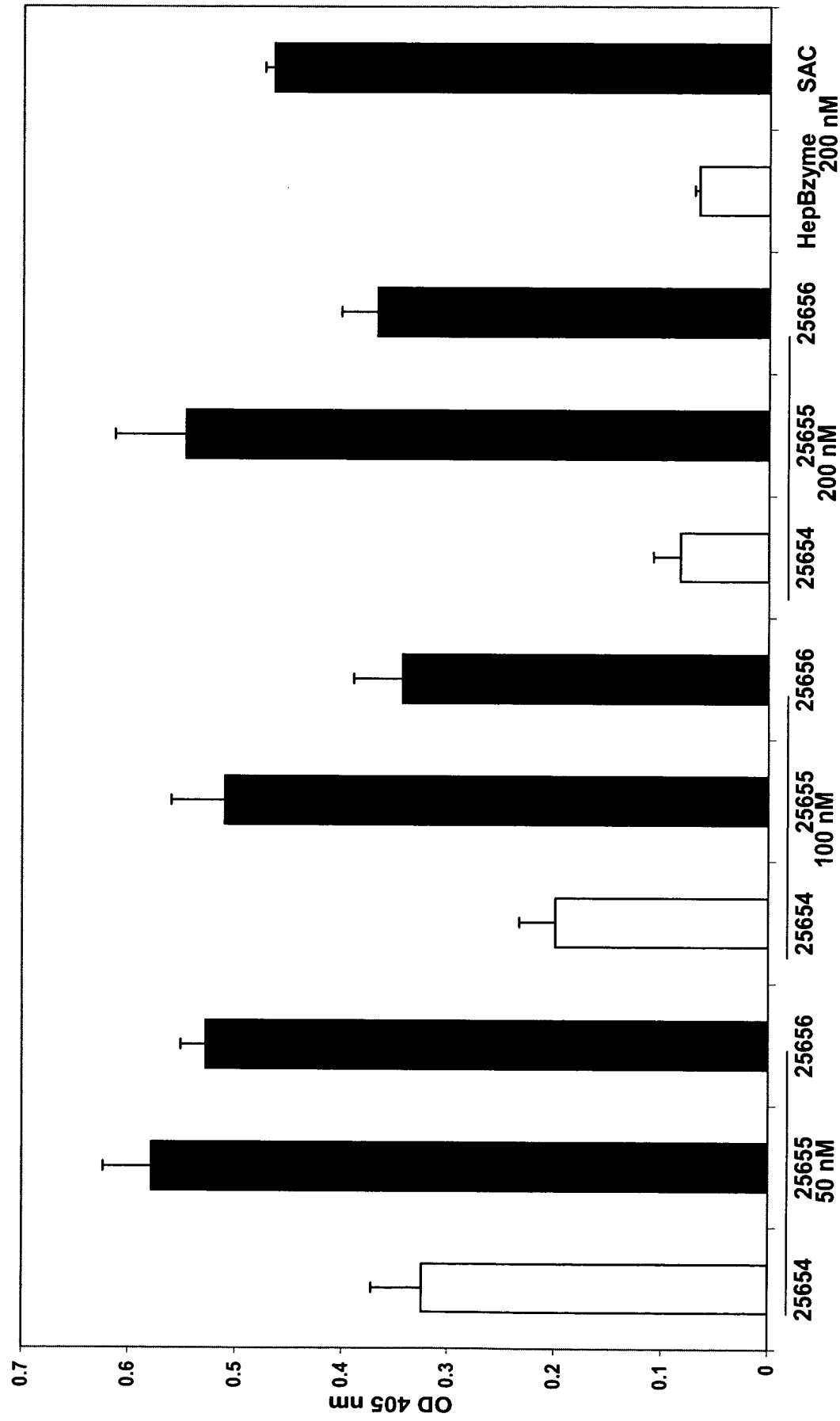


Figure 19: HBV Enhancer I Oligo Screen 400 nM: HBsAg
OD 405 nm
0
0.1
0.2
0.3
0.4
0.5
0.6
Oligos (400 nM)
25639
25640
25641
25642
25643
25644
25645
25646
25651
25652
25653
25654
25655
25656
25657
25658
HepBZyme
SAC

Figure 20: HBV Enhancer 1 Oligos Dose Response HBsAg



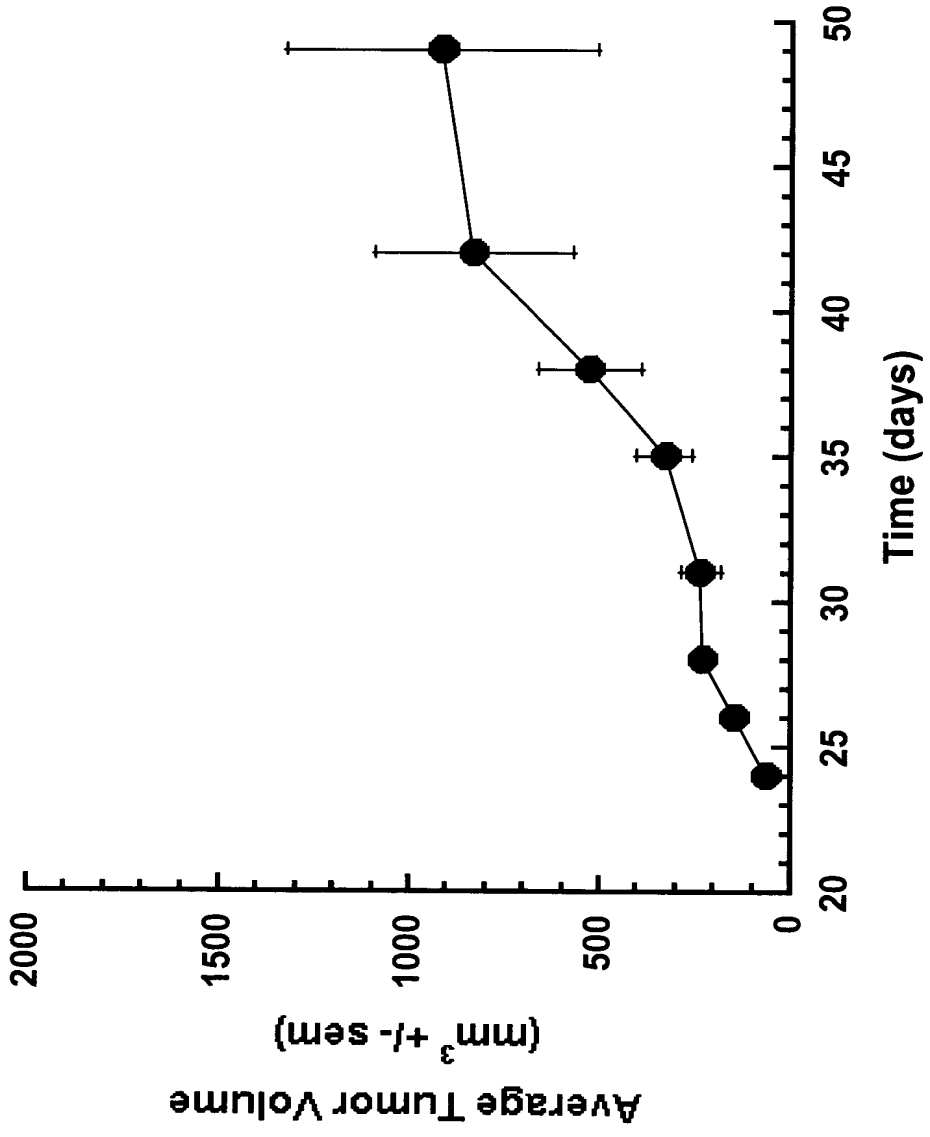


Figure 21: Growth of HepG2.2.15 tumors in Athymic Nu/Nu female mice

Figure 22: Growth of HepG2.2.15 tumors in Athymic Nu/Nu female mice

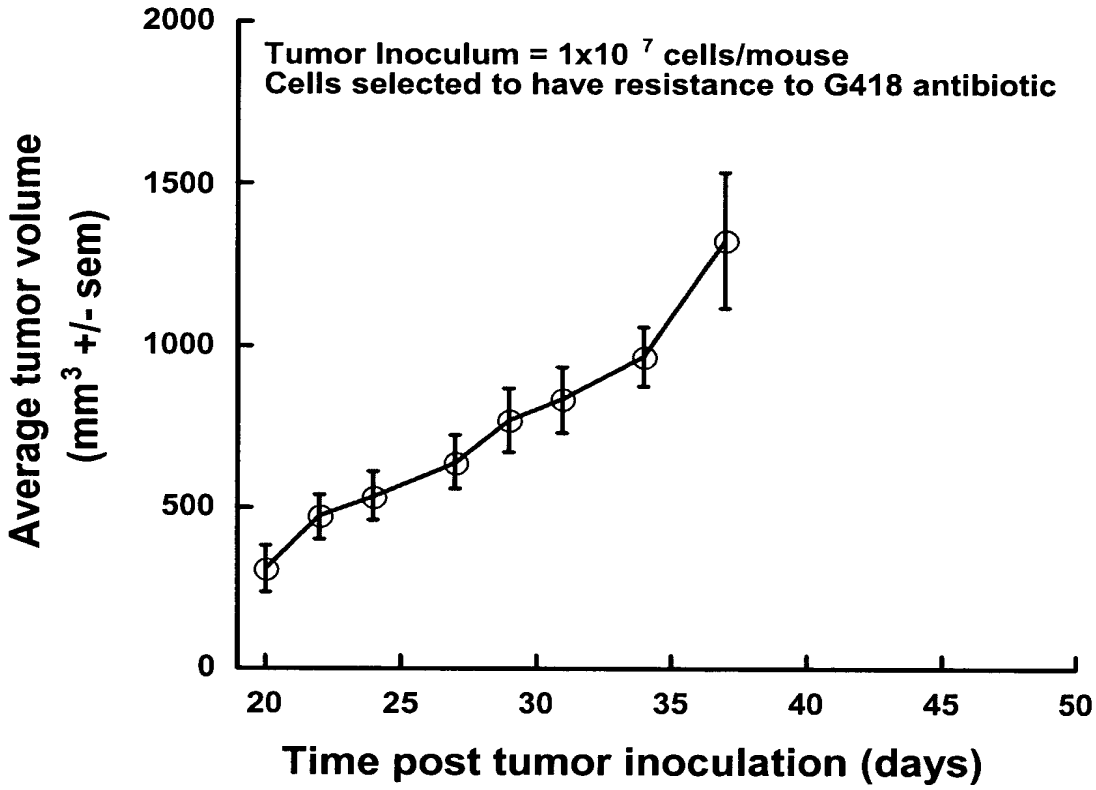


FIGURE 23 Dual Reporter System for Cytoplasmic HCV Target

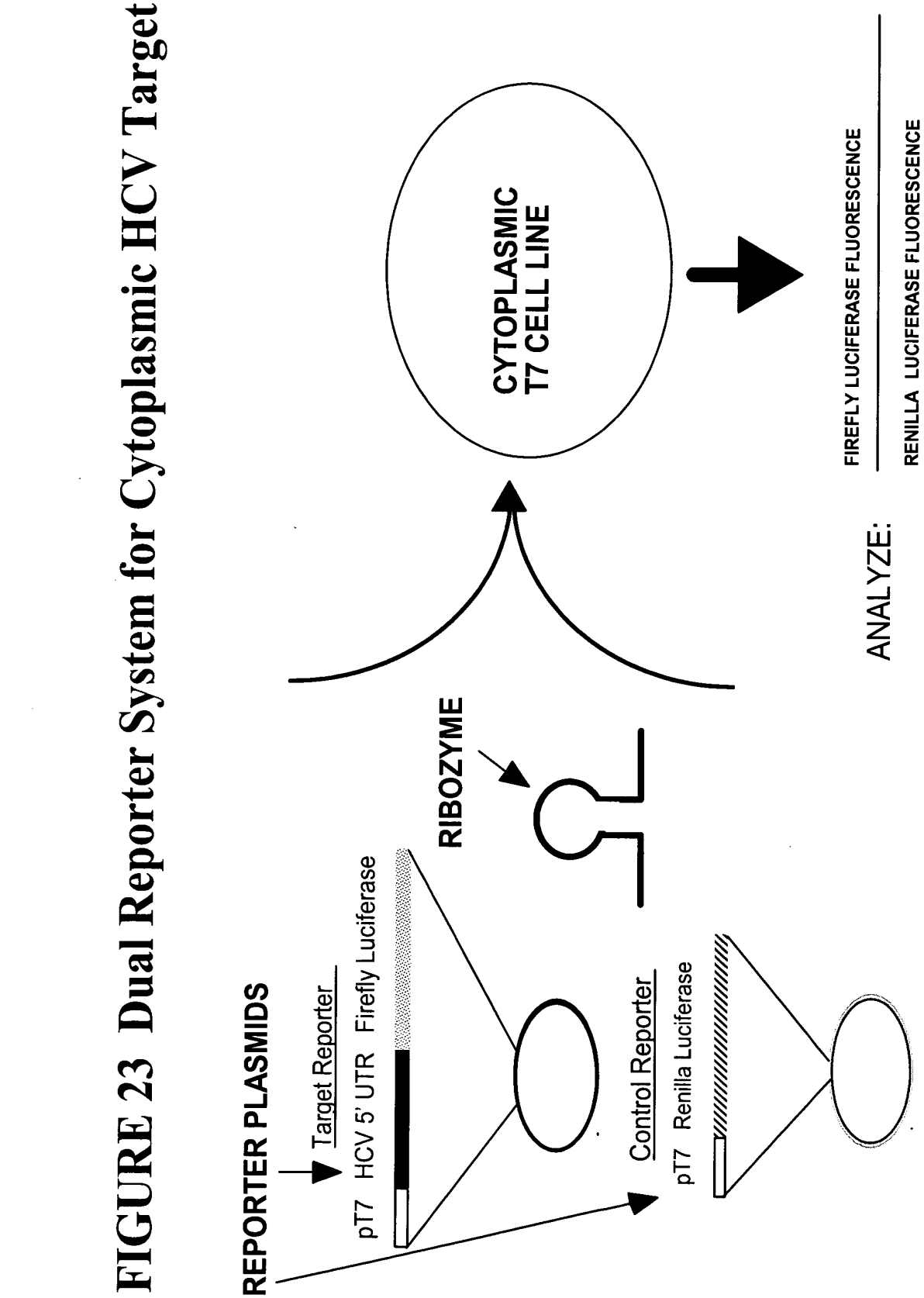


Figure 24: Secondary structure of the HCV 5'UTR

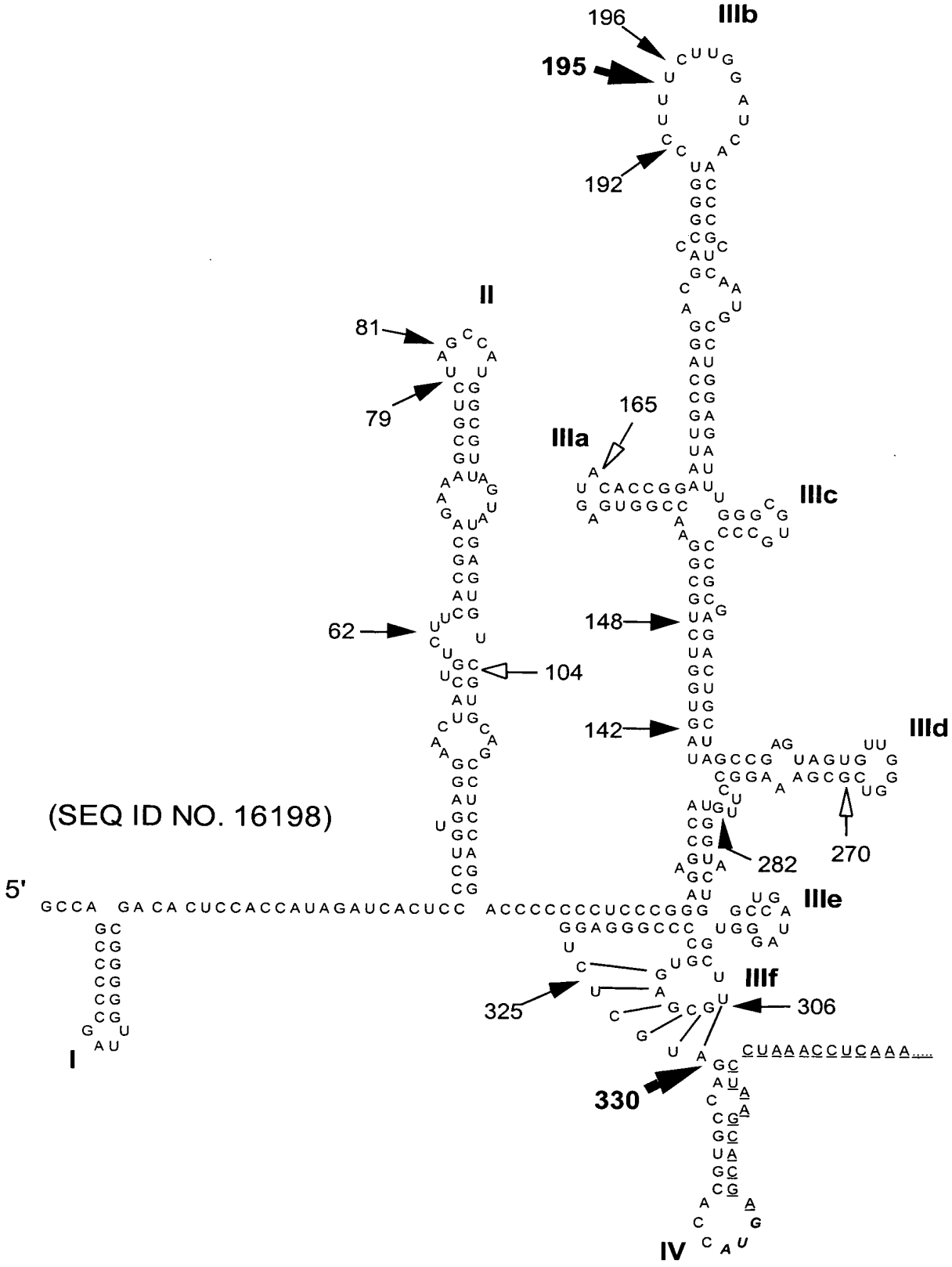
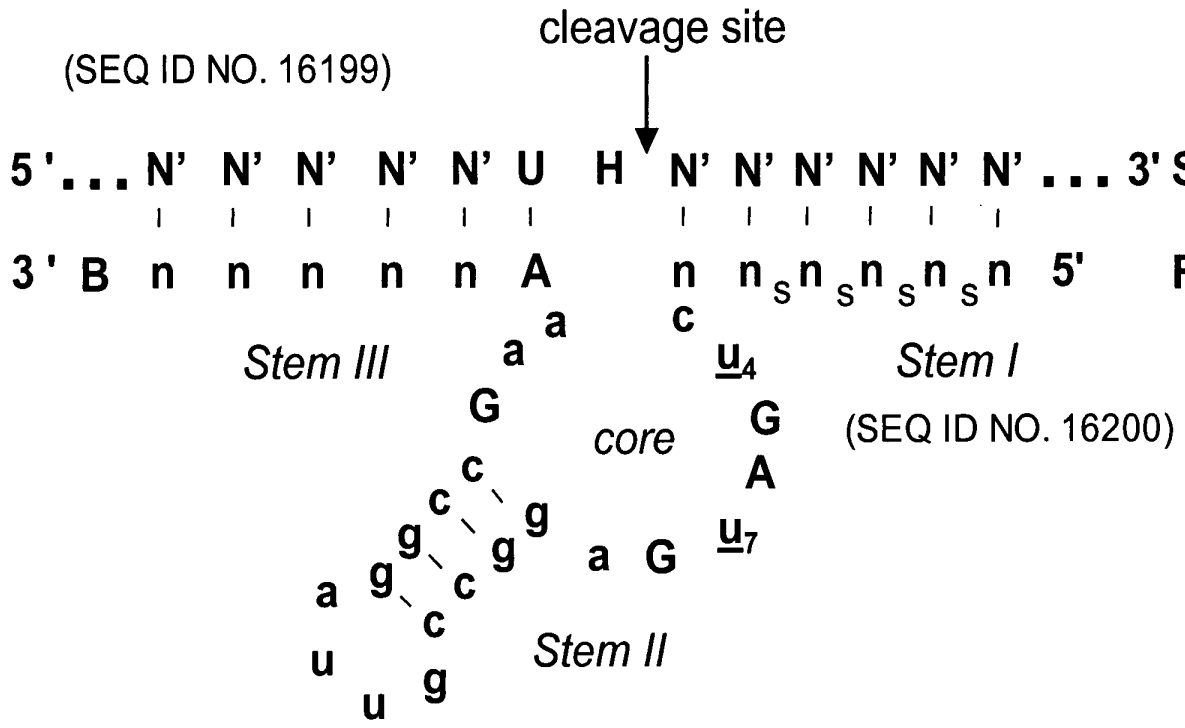


Figure 25: A Chemically Stabilized Enzymatic Nucleic Acid Molecule



UPPER CASE = RIBO nucleotide
lower case = 2'-O-methyl nucleitide
u = 2'-deoxy-2'-amino Uridine
s = phosphorothioate
B = inverted deoxyabasic moiety

Figure 26A: Enzymatic nucleic acid mediated inhibition of HCV-luciferase expression

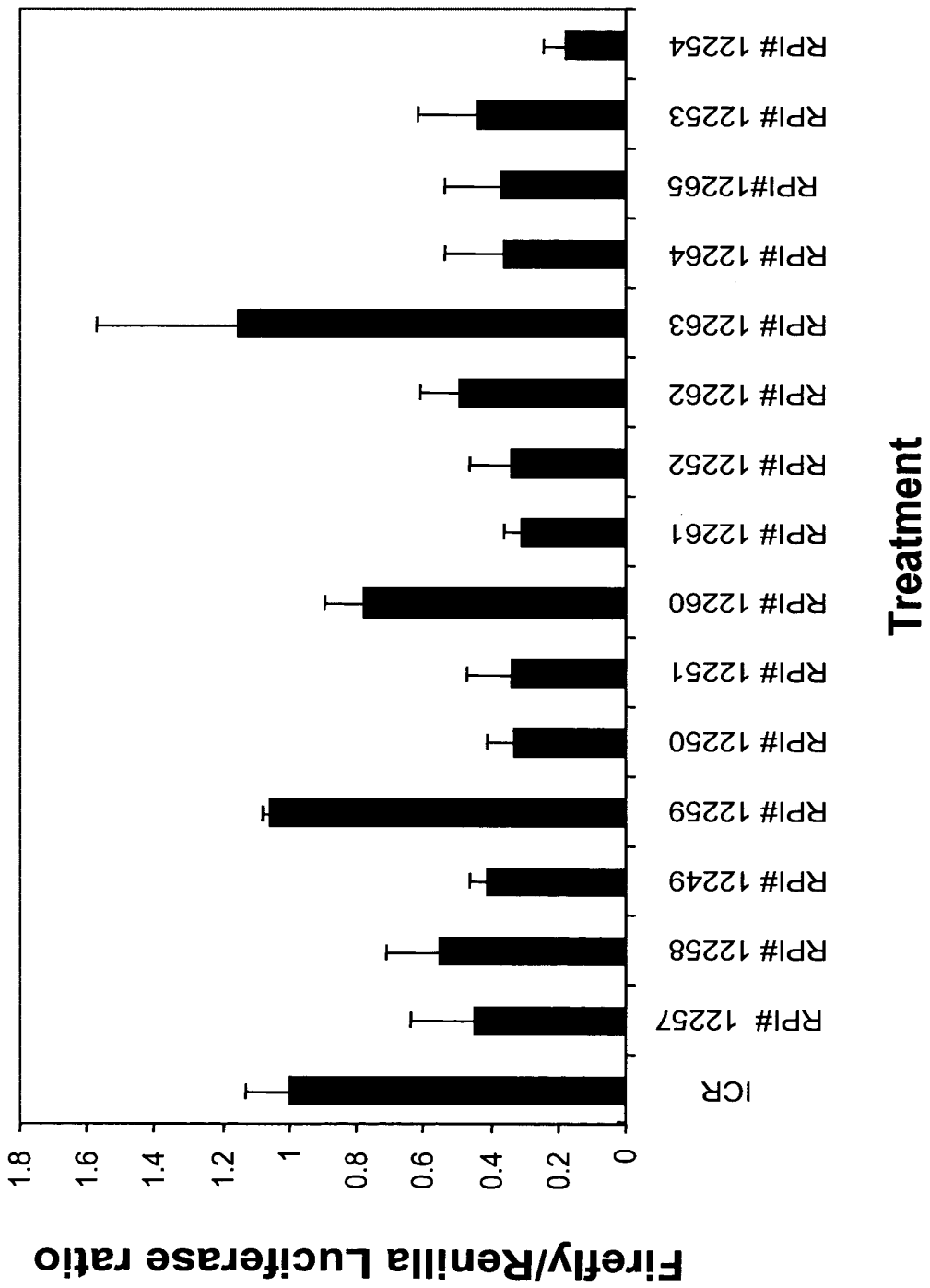


Figure 26B: Enzymatic nucleic acid mediated inhibition of HCV-luciferase expression

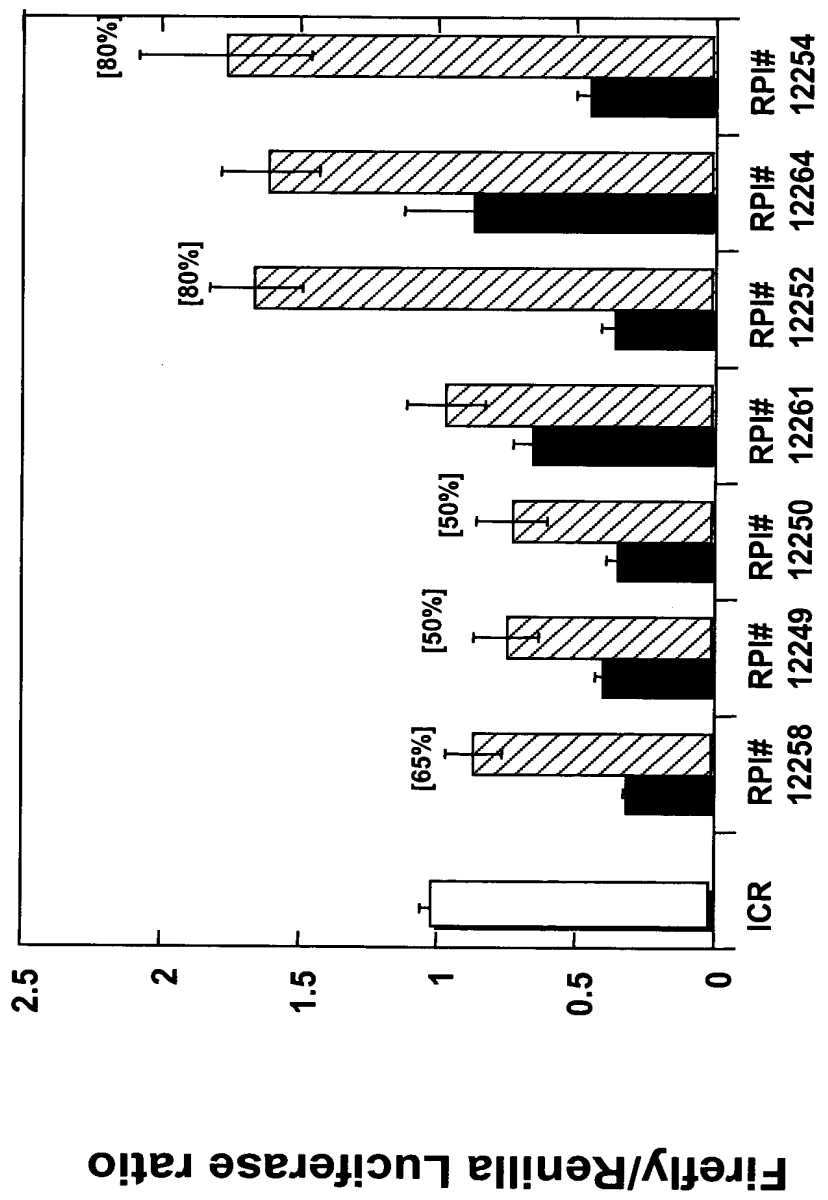


Figure 27A: Dose-dependent enzymatic nucleic acid inhibition of HCV/luciferase expression

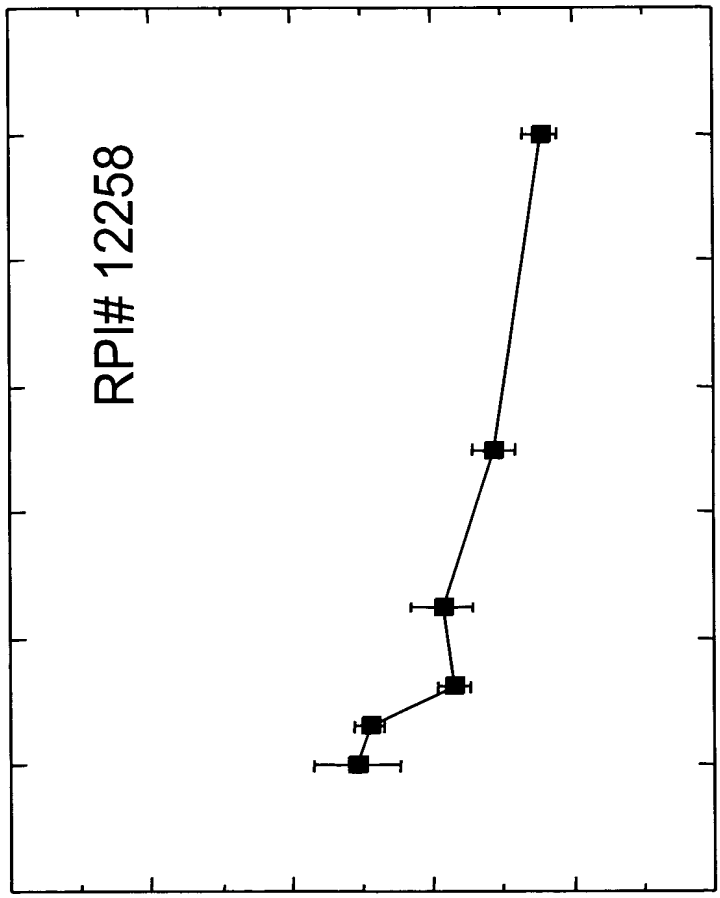


Figure 27B: Dose-dependent enzymatic nucleic acid inhibition of HCV/luciferase expression

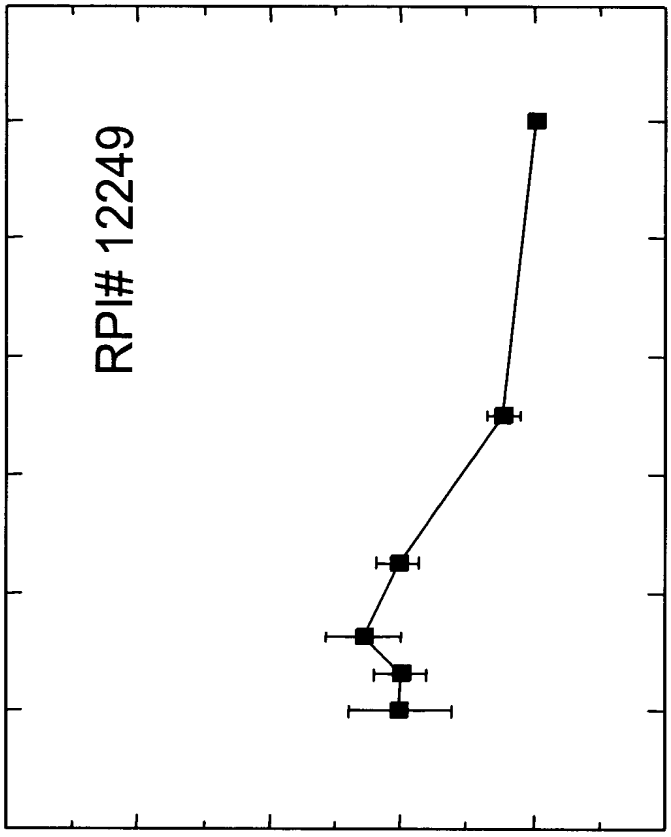


Figure 27C: Dose-dependent enzymatic nucleic acid inhibition of HCV/luciferase expression

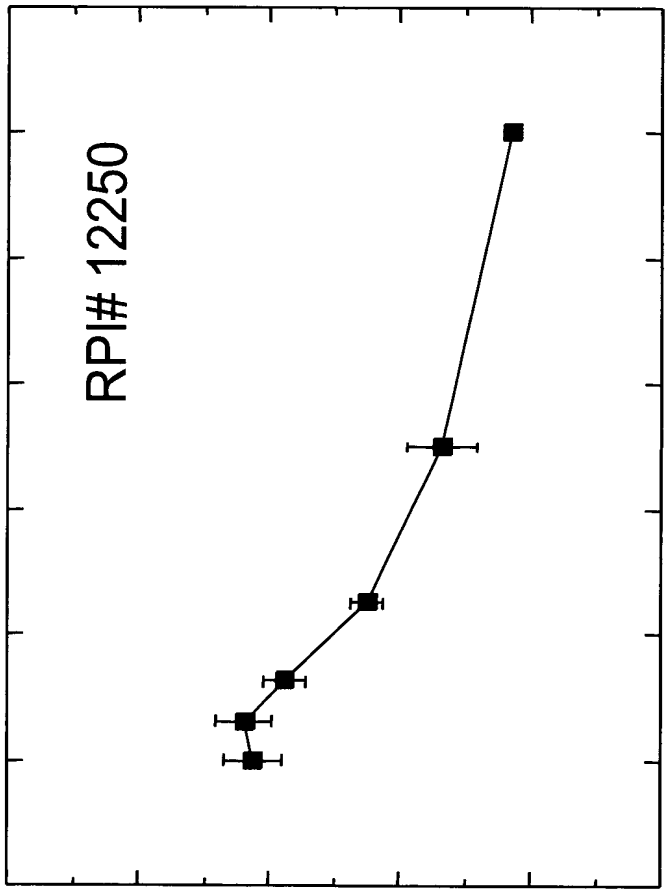


Figure 27D: Dose-dependent enzymatic nucleic acid inhibition of HCV/luciferase expression

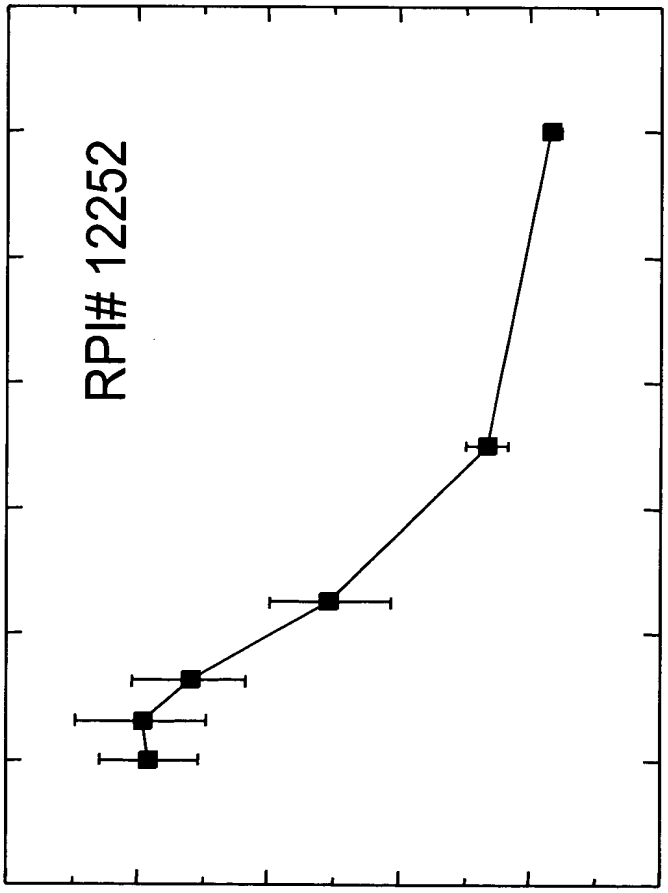


Figure 27E: Dose-dependent enzymatic nucleic acid inhibition of HCV/luciferase expression

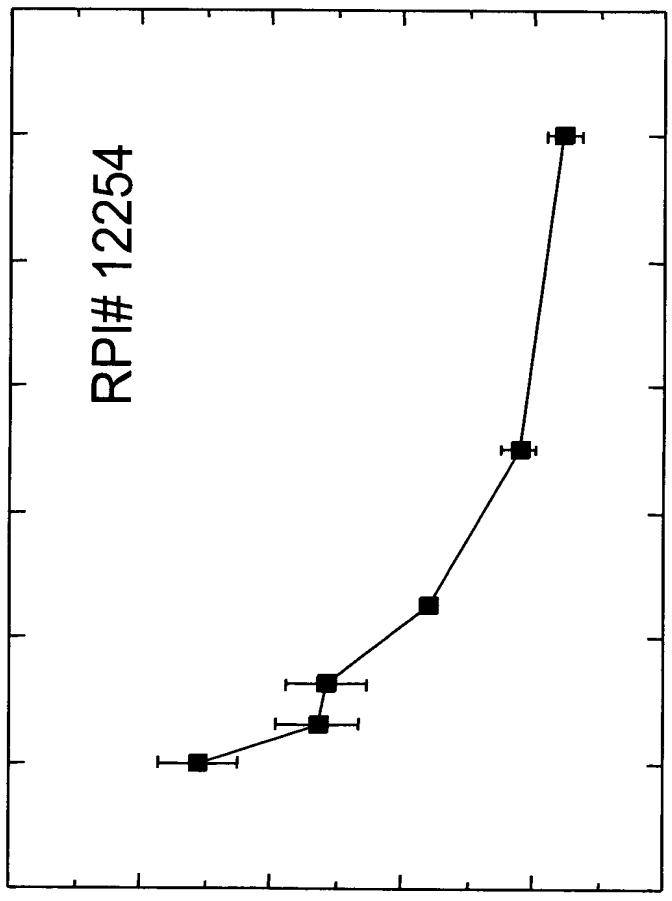


Figure 28A: Enzymatic nucleic acid reduction of HCV/luciferase RNA and inhibition of HCV-luciferase expression

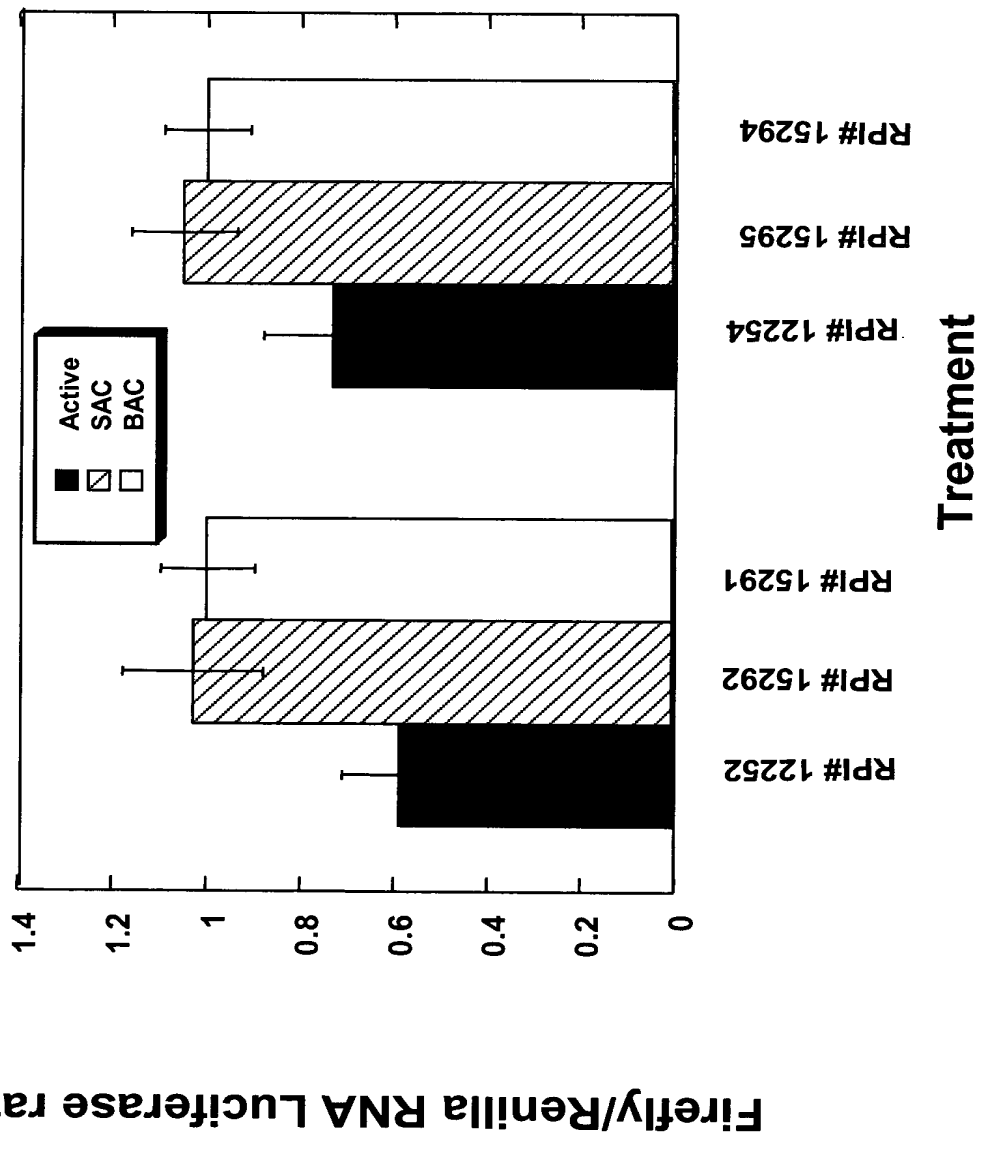


Figure 28B: Enzymatic nucleic acid reduction of HCV/luciferase RNA and inhibition of HCV-luciferase expression

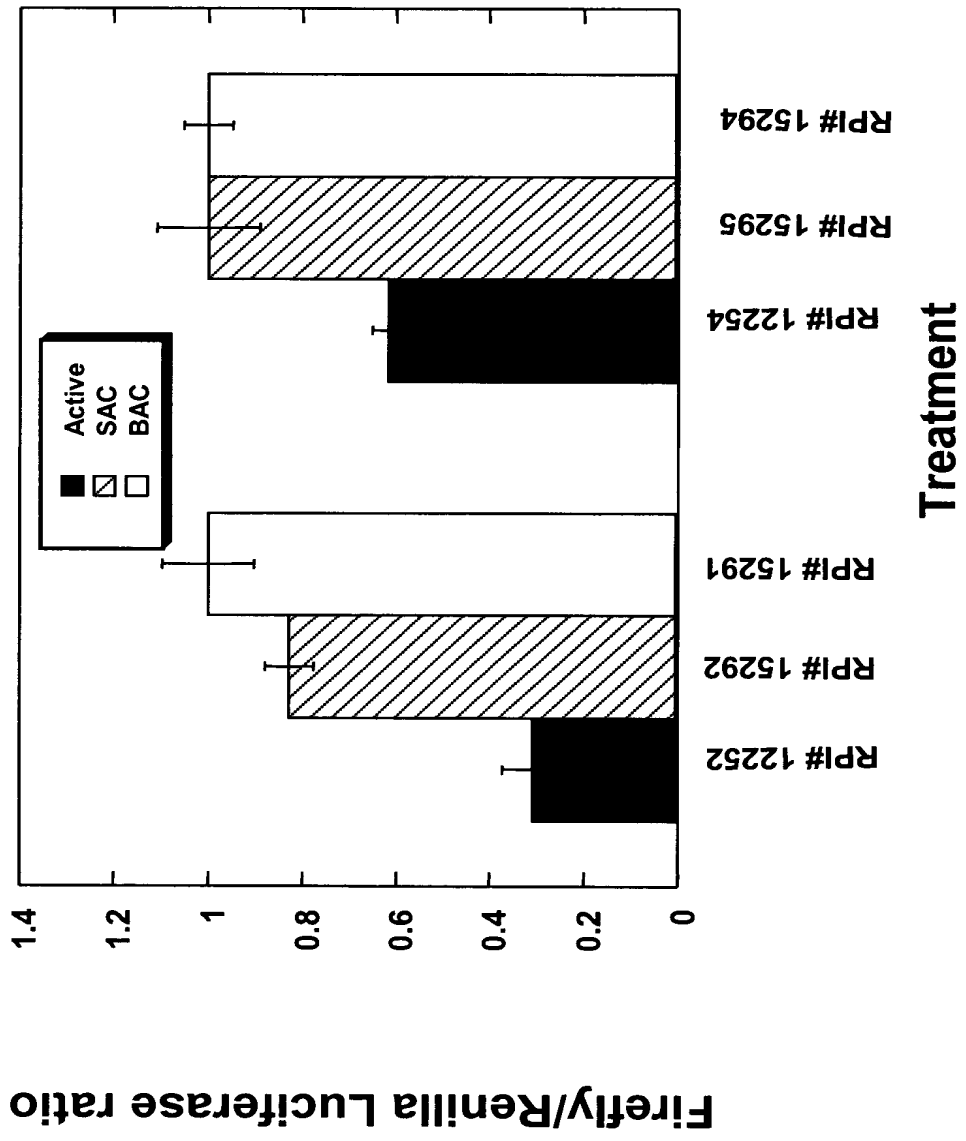


Figure 29A: Interferon Dose response with Enzymatic Nucleic Acid

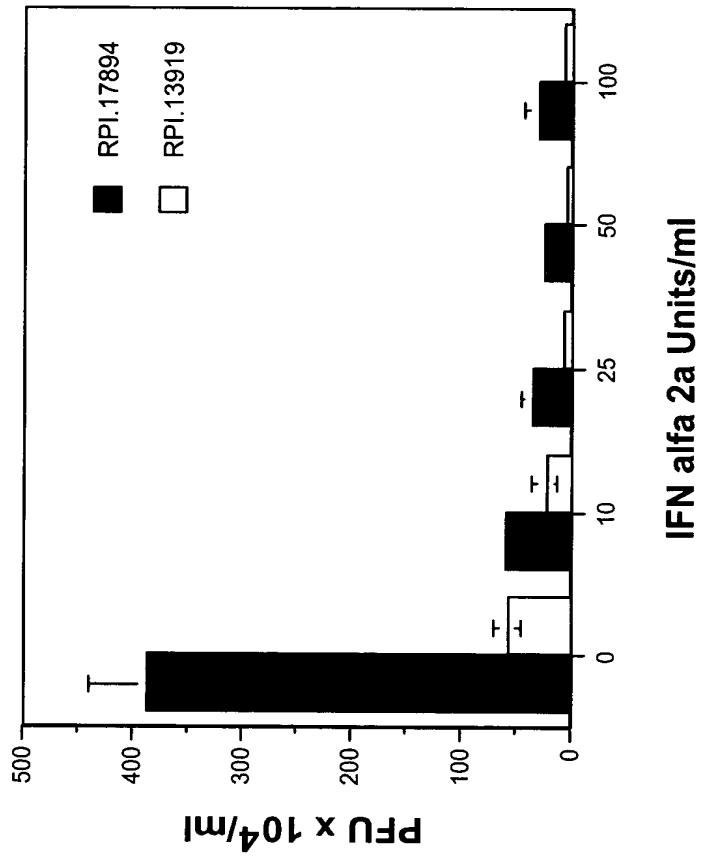


Figure 29B: Interferon Dose response with Enzymatic Nucleic Acid

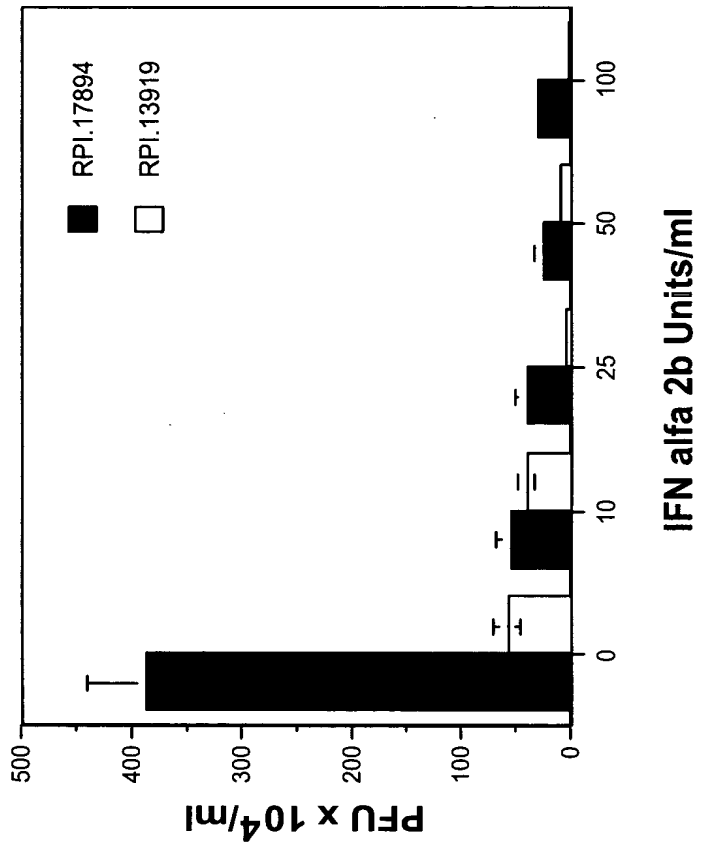


Figure 30: Site 195 anti-HCV enzymatic nucleic acid dose response in combination with interferon pretreatment

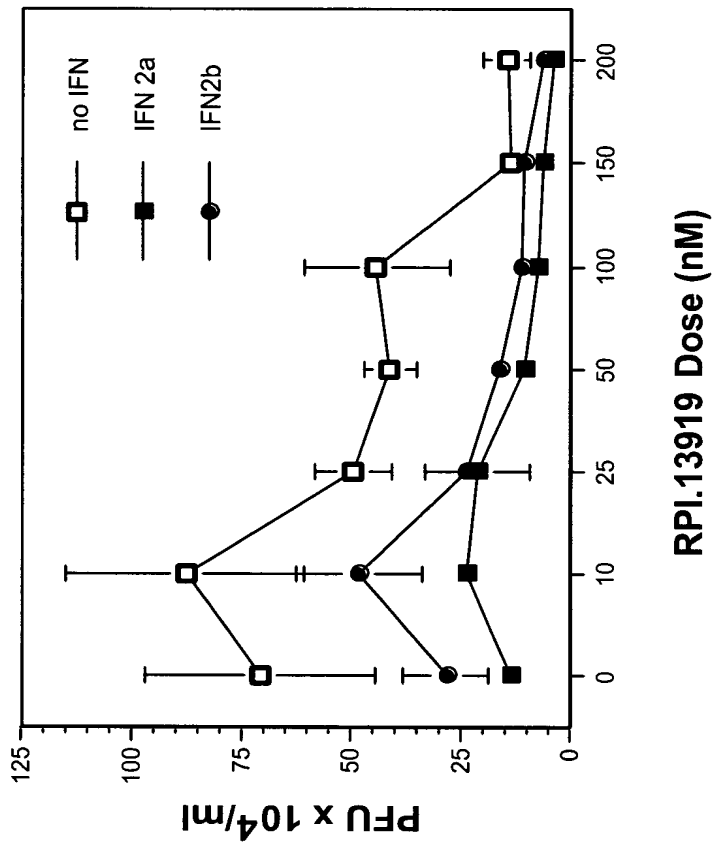


Figure 31A: CIFN dose response with site 195 anti-HCV enzymatic nucleic acid treatment

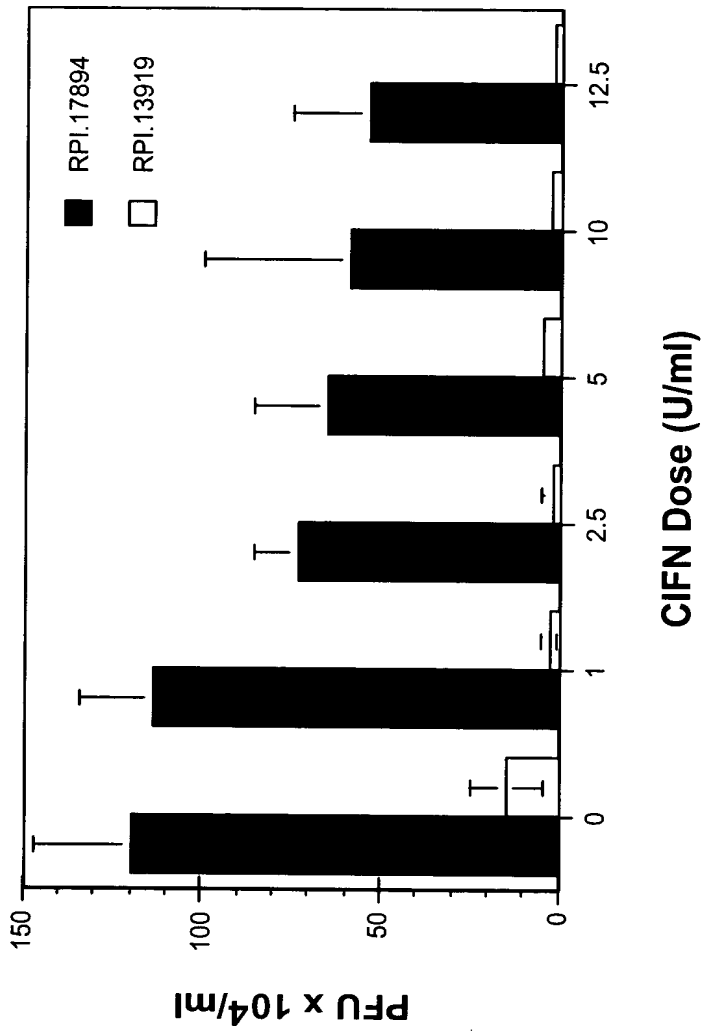


Figure 31B: Site 195 anti-HCV enzymatic nucleic acid dose response with CIFN pretreatment

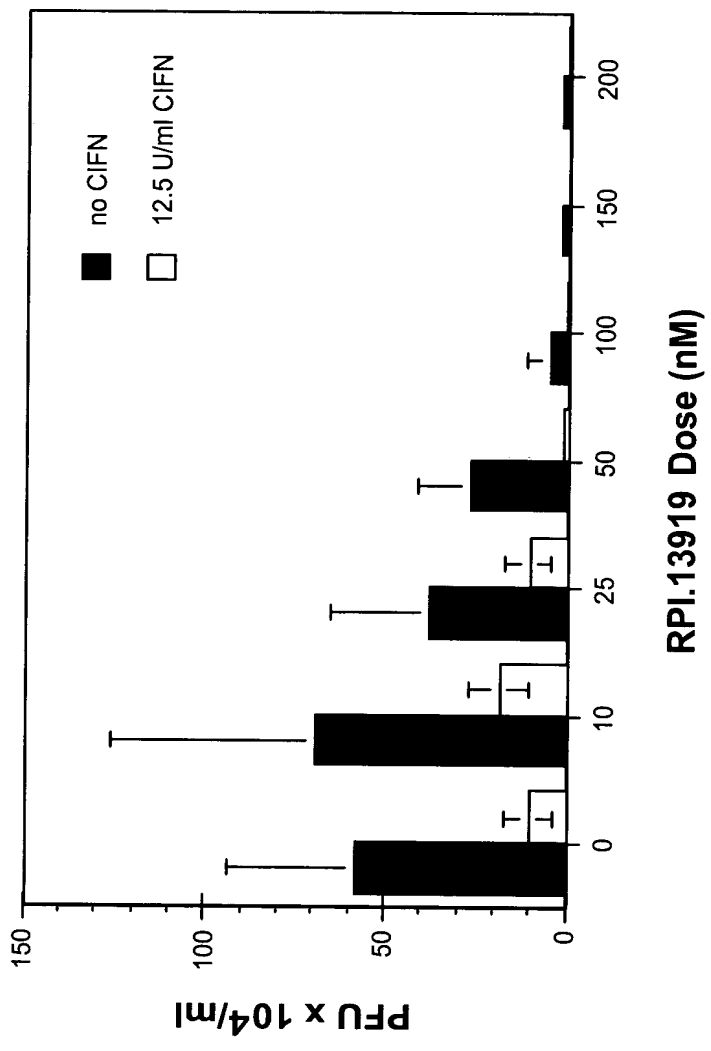


Figure 32: Enhanced antiviral effect of an anti-HCV enzymatic nucleic acid targeting site 195 used in combination with consensus interferon (CIFN)

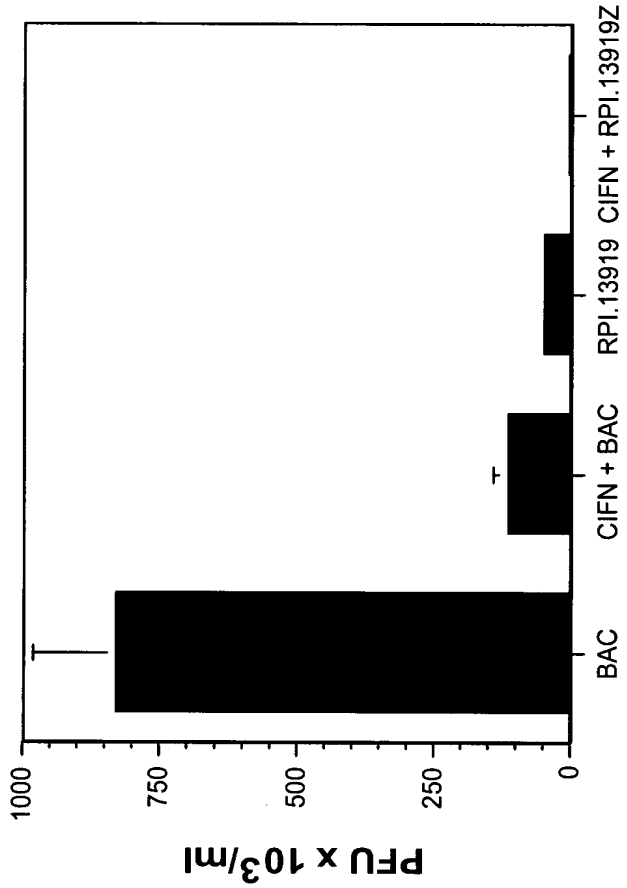


Figure 33: Inhibition of HCV-PV Replication by Zinzyme Treatment

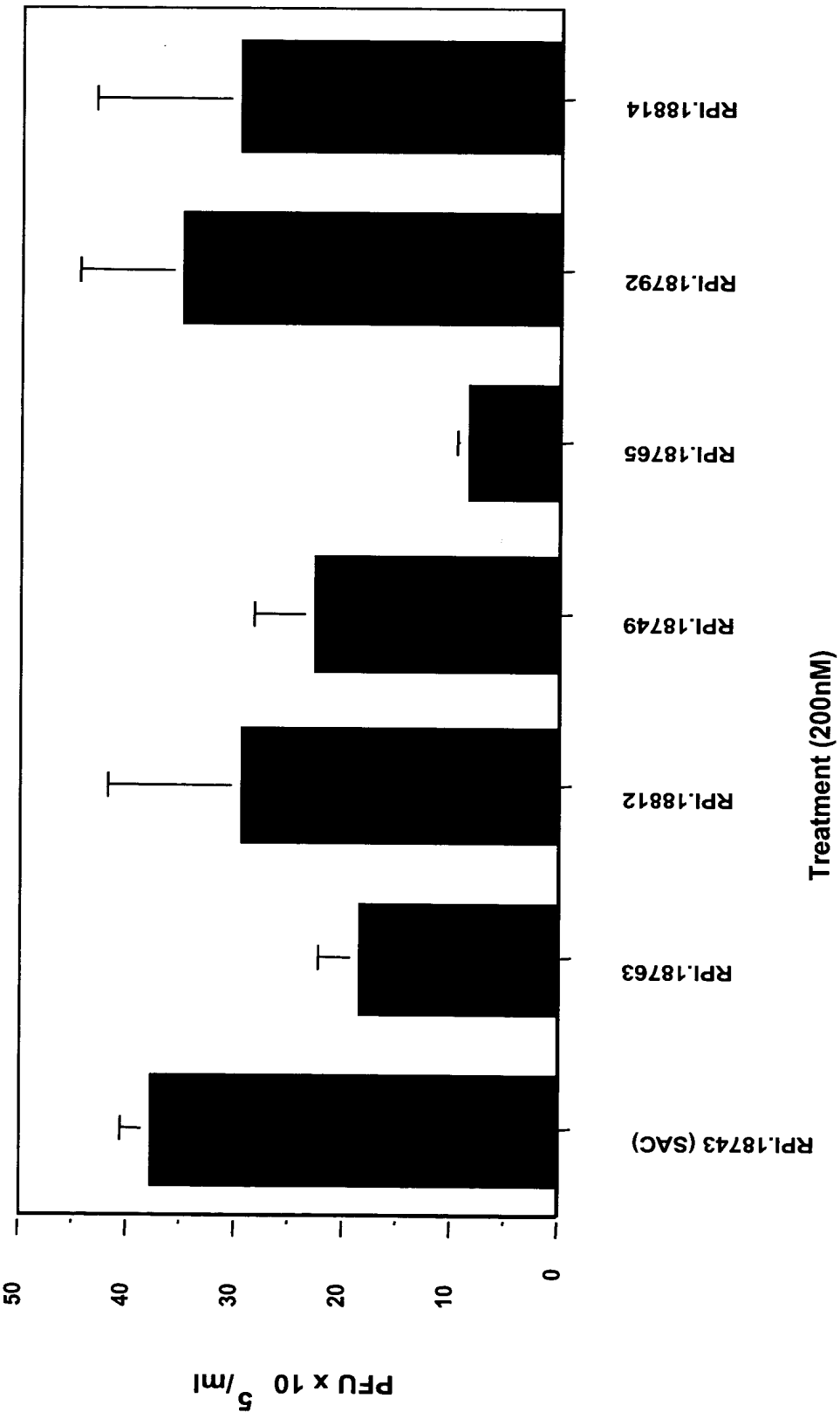


Figure 34: Inhibition of HCV-Poliovirus Replication by Antisense

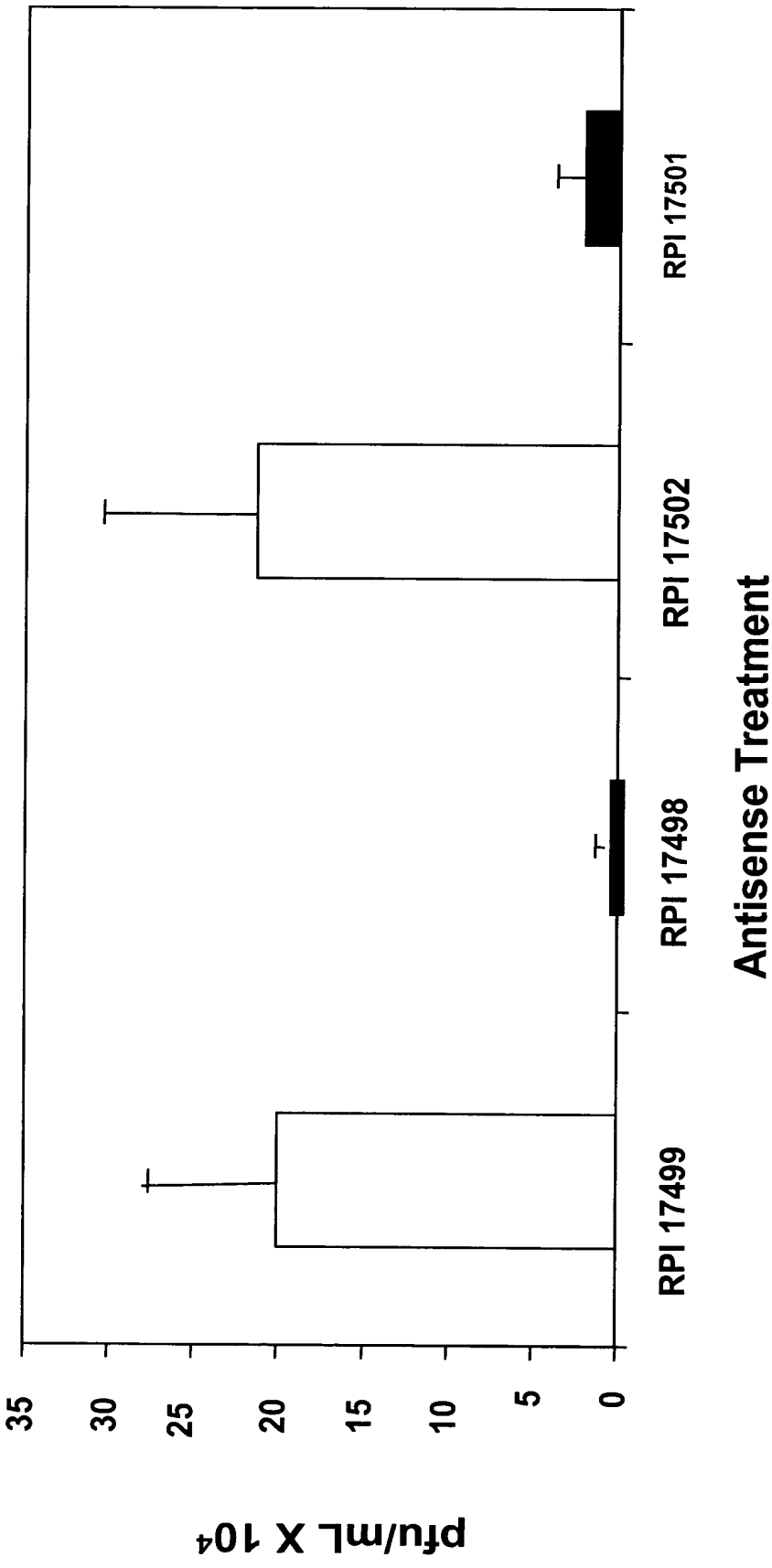
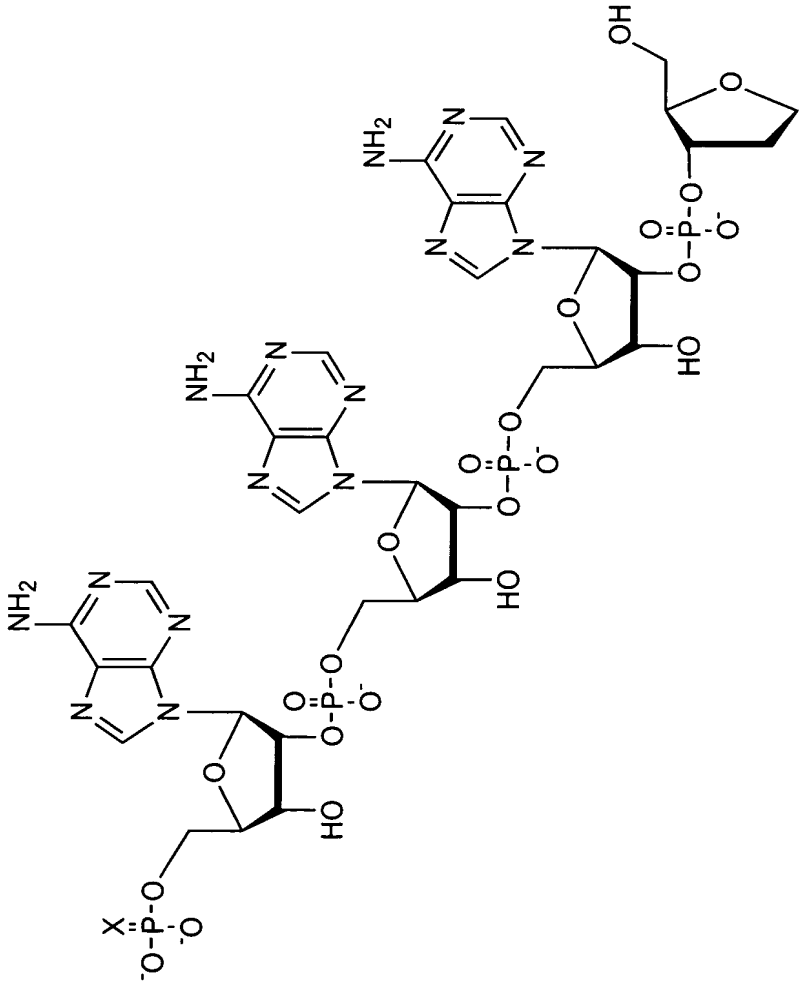


Figure 35: Modified 2-5A Compound



I: X = O
II: X = S

Figure 36A: Ribozyme activity and enhanced antiviral effect

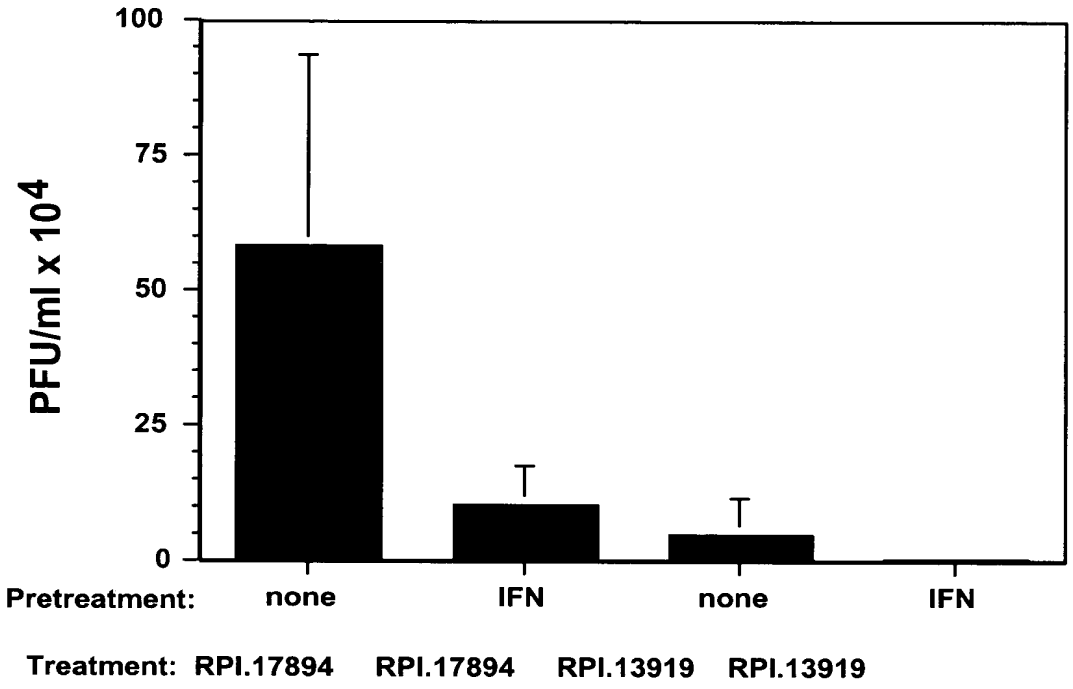


Figure 36B: Ribozyme activity and enhanced antiviral effect

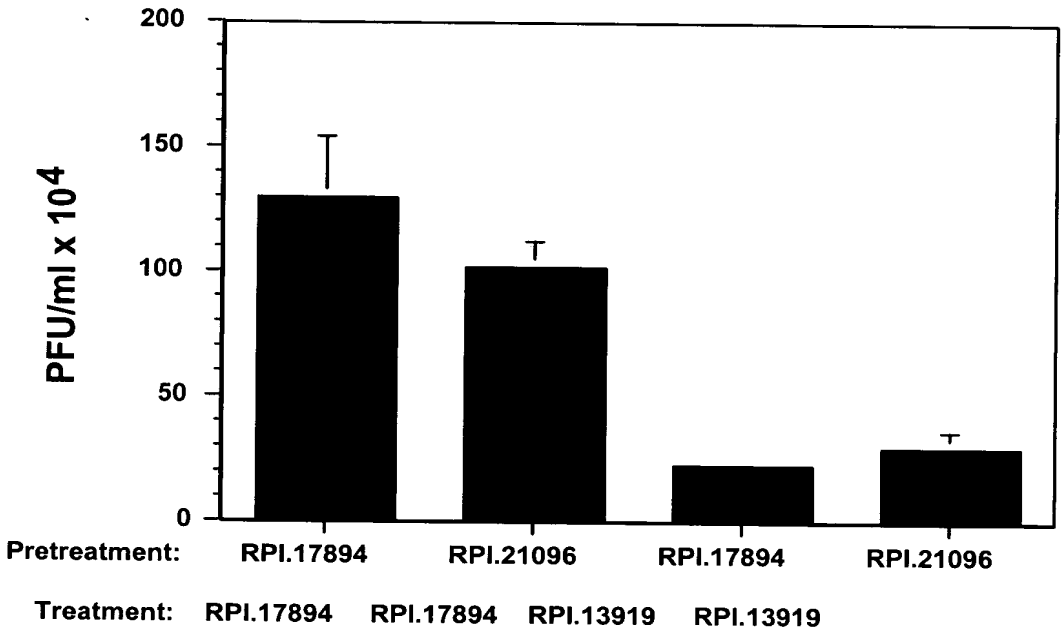


Figure 37: Inhibition of viral replication with anti-HCV ribozyme or 2-5A treatment

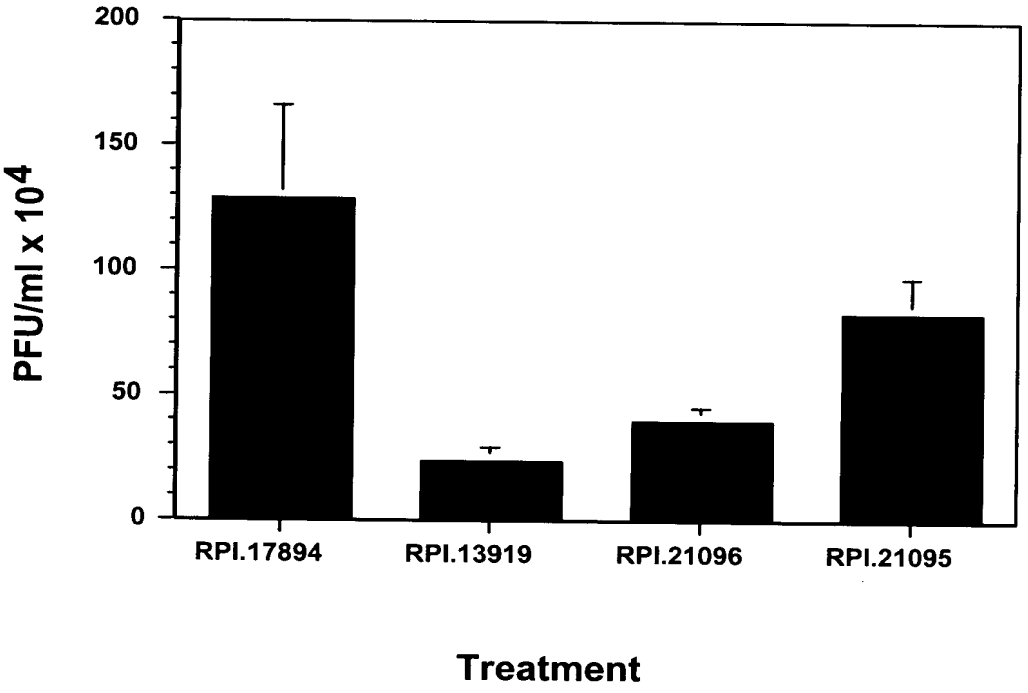


Figure 38: Anti-HCV ribozyme in combination with 2-5A treatment